LUNG GROWTH IN ADOLESCENT MEN

A THESIS SUBMITTED TO THE UNIVERSITY OF SURREY
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BY

NICOLA G ROBINSON B.Sc

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ERGONOMIC RESEARCH UNIT
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SUMMARY

Lung growth as determined by changes in lung volumes in adolescent men aged 17-19 years is poorly documented in the literature. This study was designed to investigate lung growth in a population of shipyard workers.

One hundred and ninety eight apprentices participated in a longitudinal study. Lung volumes including FRC by helium dilution and anthropometric measurements including thoracic dimensions were obtained.

In this growing population, lung growth exceeded the growth in stature. The subdivisions of TLC showed a greater increase in FRC than IC and was shown not to be due to lowering of the diaphragm. Lung growth was associated with an increase in the thoracic dimensions which contributed to the description of lung size in this age group.

To determine whether the elastic properties of the respiratory system may have contributed to the change in the thoracic dimensions and lung growth, a cross-sectional study was undertaken. Two subgroups of men were selected from the longitudinal study; one group had large lung volumes, the other small lung volumes. Static lung compliance and elastic recoil were measured and tracheal dimensions obtained from chest X-rays.

The level of physical activity reported by each individual was not associated with their lung size; neither was their respiratory muscle strength as measured by maximal respiratory pressures. Lung growth was not associated with changes in lung elasticity, although men with larger lungs did have more distensible lung tissue. There was no correlation between lung and tracheal size in agreement with the concept of dysanaptic growth \((r = 0.16; \ p > 0.05)\)

It was concluded that growth of the chest wall, with the consequent increase in thoracic dimensions, was accompanied by an increase in lung volume \((r = 0.52; \ p < 0.05)\). The lung developed within the enlarged thoracic cavity by actual tissue growth rather than expansion of existing structures.
ACKNOWLEDGEMENT

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CHAPTER 1

ANATOMICAL GROWTH AND DEVELOPMENT OF THE LUNG
1.1 Introduction

The lung is the organ of the respiratory system which performs the vital functions of ventilation and gas-exchange. If the organism is to survive the lung must be sufficiently mature at birth to carry out this function adequately.

In utero the lung develops in an aqueous environment as the maternal blood supply provides all the respiratory needs of the growing foetus via the placenta. Although surrounded by amniotic fluid, the foetal lung, as if in anticipation of the traumatic events to take place at birth, develops the structures necessary for gaseous exchange. In the human, the lung is capable of gas-exchange from about the 28th week of gestation. At term, the respiratory system encounters little difficulty with the onset of air breathing. After parturition, the lung continues to develop in accordance with the needs of the growing body tissues. It is, however, not true to say that the lung at birth is a miniature of that found in the adult. Post-natally the lung develops in structure and grows in size until full maturation when it is considered a highly complex and proficient gas-exchanging organ.

The growth of the lung is truly prolific; from a lung bud in the human embryo 5mm in length the lung develops to have an internal surface area forty times that of the body surface area (17). This development has been described from careful documentation of the changes occurring in the various constituents of the human pulmonary system; notably the airways, alveoli, pulmonary vasculature and lung parenchymal tissue, throughout pre- and post-natal life. Much of these data have been obtained in animal species and it is important to be aware of this when attempting to extrapolate the findings to man. The phases of growth shown by other species may follow the same pattern as human development but they are more difficult to interpret. Similar note should be taken when discussing data from animal experimentation. Certain experiments, particularly into factors controlling lung growth, intrinsically involve alterations in body size (154). In spite of these reservations, however, a great deal of importance is
attributed to animal data when describing human growth of the lung.

This chapter considers the anatomical and physiological changes which determine the growth and development of the lung, concentrating on the major features of the respiratory system. Later the functional consequence of this physiological development will be critically discussed, with particular reference to the post-natal period 17-19 years.

1.2 Embryological Development

1.2.1 Gross Anatomical Development

The lung first appears on the 26th day of gestation as a ventral diverticulum arising from the caudal end of the laryngeotracheal groove. It is lined by endodermal epithelium and invested by splanchnic mesenchyme. The embryological formation of the diaphragm is complete by the end of the 7th week of gestation when the abdominal organs develop a ventral mesodermal fold called the septum transversum (29). The Commission on Embryological Terminology (1970) (110) have described four stages of lung development, although investigators may differ in their interpretation of the exact timings of each stage. Generally the pattern of lung growth may be represented by the embryonic (conception to 7 weeks), pseudoglandular (7-16 weeks), cannicular (16-26 weeks) and terminal sac periods (26th week to term). The latter has replaced the term alveolar period as true alveolar development is now considered to be an exclusively post-natal event (101).

The pseudoglandular period is so called because the lung sacs, which give rise to the lobar buds, have the histological appearance of a gland until about the 17th week of gestation. There after, up to the 24th-26th week, the cannicular period is typified by the canalisation of the respiratory portion of the tracheobronchial tree. In this stage, the intrusion of the pulmonary vasculature creates the blood-gas interface. It is during the cannicular period that the respiratory units or acini are first recognised.
The acinus may be described as the portion of airway capable of gas-exchange and is directly supplied by the terminal bronchiole. The terminal sac period, from the 26th week of gestation to term, incorporates the completion of canalisation and the appearance of terminal clusters of airways termed saccules. These saccules have a blood-gas barrier and will eventually lead to the post-natal development of adult alveoli. The lung at birth, therefore, has not only the capability of gas-exchange to sustain life, but also the capacity to enlarge and modify existing structures.

1.2.2. **Surfactant Production**

During the cannicular period another important phenomenon occurs, apart from the process of canalisation. This is the presence of laminar bodies in the cytoplasm of the secretory cells lining the developing airway (type II pneumocytes) (107). These laminar bodies are responsible for the production of the surfactant phospholipid lecithin (dipalmitoyl phosphatidylcholine; DPC). There are two main pathways for the synthesis of lecithin: the cytidine diphosphate choline (CDP – choline) pathway and a stepwise methylation pathway of phosphatidylethanolamine. The latter pathway is more prominent during foetal development, whereas the CDP-choline pathway is more productive in the infant and adult lung. Though accepted widely there is still some conjecture about this (121). Whatever the relative merits of these pathways there is a gradual increase in the number and size of the laminar bodies and, therefore, the synthesis of lecithin during the cannicular period. At the same time the alveolar lumen is filled with an electrolyte fluid which is a specific secretion of the lung and not simply aspirated amniotic fluid. This foetal lung liquid (FLL) facilitates the opening of the lung since the critical opening pressure of a fluid-filled lung is less than that of a collapsed lung, a clear mechanical advantage for the first breath at parturition. The purpose of the pulmonary surfactant is to form a surface film lining the saccules, to stabilise the alveolar membrane by decreasing its surface tension.
Surfactant cannot achieve its effect by remaining within the epithelial cells, so it is secreted into the fluid-filled spaces of the alveolar lumina (32). The FLL which is extruded into the amniotic fluid contains pulmonary surfactant from the beginning of the terminal sac period. There is a sharp rise in the secretion rate at about the 29th week of gestation from which time until term the rate diminishes. However, there is no reason to presume a fall in the rate of production. This late gestational accumulation of surfactant in the cytoplasm of the endothelium cells is in preparation for the onset of breathing at parturition. With the first few breaths the FLL is cleared by absorption into the rapidly increasing pulmonary blood stream and drainage into the perivascular lymph spaces. Apparently, the apoprotein-phospholipid complex of the surfactant molecules cannot cross the epithelial barrier and thus remain in the alveolar surface film. The surfactant molecules orientate themselves in such a way that the hydrophobic radical lies in the gas phase and the hydrophilic radical remains in the liquid phase. In this way there is widespread interruption of the surface film by the surfactant molecules so reducing the surface tension of the alveolar membrane.

The foetal lung anatomically is capable of gas-exchange from the 28th week of gestation. In order to survive premature parturition this mechanism of ensuring the stability of the alveolar membrane must also be capable of functioning at this time. There is a negligible time delay between the secretion of surfactant by the type II pneumocytes and the appearance of surfactant in the amniotic fluid. The concentration of surfactant in the amniotic fluid can, therefore, be used biochemically to assess the maturity of the alveolar membrane and the ability of the foetus to endure the trauma of parturition (66). Post-natally, there is a constant level of surfactant presumably reflecting a balance between its synthesis and degradation.
1.3 Tracheobronchial Tree Development

1.3.1 Conducting Airways

By the time the pseudoglandular period begins at about the 16th week of gestation, all the bronchopulmonary segments of the tree are detectable under the microscope and cartilage is found in the trachea. The distal airways bifurcate, in a markedly acute fashion, as they continue to divide and grow. There is an acceleration in this dichotomous behaviour between the 10th and 14th weeks of gestation, at which time it is reported that 70% of the bronchial branching is complete (26). The left lung sac has a greater number of pre-segmental bronchial pathways than the right lung sac which develops intrasegmental bronchi earlier. The right lung sac also has one to five more generations of intrasegmental bronchi by the 14th week of gestation but after this there appears to be no significant difference between the intrasegmental bronchial pathways in either lung sac. By the end of the pseudoglandular period (16th-17th week) all the non-respiratory bronchial pathways have been formed and are represented as blind tubules lined with cuboidal or columnar epithelium (81).

Cartilage is present in the trachea and main bronchi by the 10th week of gestation but does not follow the pattern of growth displayed by the airways of the bronchial tree. There is no spurt in development, characteristic of the bronchial tree between the 10th and 14th weeks of gestation. The formulation of cartilage lags behind the extension of branching airways and, therefore, continues well into the canicular period when the number of non-respiratory branching airways remains constant. At the 24th week of gestation cartilage is absent from between three and nine of the most distal generations which, by definition, only allows an increase in the number of bronchioles in later foetal life. There is an apparent relationship between the length of the bronchial pathway and the extent to which cartilage is present in the generations of airways; the
longer the axial pathway the greater the number of cartilaginous airways (26).

At the end of the pseudoglandular period all the non-respiratory or conducting airways are present (15-26 along an axial pathway) (128). The future foetal development of the tracheobronchial tree is primarily devoted to the respiratory portion of the airway or acinus. Although no further conducting airways develop after the 16th week of gestation, growth continues with an increase in the diameter and length of the existing branches: the major airways increasing 3-4 times in diameter up to the age of 10 years (21). There is some debate as to whether this pattern of hypertrophic growth is dysanaptic (68, 88) (different branches of the airways grow at different rates) or isotropic (169) (equal relative increases in the linear dimensions).

1.3.2 Gas-Exchanging Region

Since it is imperative that the gas-exchanging region of the lung is adequately developed at term, the acinus develops rapidly from the beginning of the cannicular period (Fig 1.1). At this time the most distal airway which constitutes the acinus is only 0.1mm in length. By the 19th week of gestation it has lengthened and divided to produce two or more respiratory bronchioles. These bronchioles are the first order of gas-exchanging airways and their walls are lined on the arterial side with columnar or cuboidal epithelium, the other side being lined with flattened epithelium (12). The terminal bronchiole wall has become thinner but is still entirely lined with cuboidal or columnar epithelium. It is at this stage that the acinus becomes recognisable; it becomes vascularised with pulmonary capillaries. After the 19th week the most distal airways continue to lengthen and by the 24th week of gestation one or two terminal ducts have formed. These are short, straight airways completely lined with flattened epithelium and at this stage the acinus is reported to be 0.6mm in length. During the terminal sac period, in the final stage
FIG. 1.1 SCHEMATIC REPRESENTATION OF THE GROWTH OF THE ACINUS

A subpleural one is illustrated


<table>
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<th>Age</th>
<th>Length from TB to pleura</th>
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| (a) 16 wks gest. | 0.1mm
| (b) 19 wks gest. | 0.2mm
| (c) 26 wks gest. | 0.6mm
| (d) birth     | 1.1mm
| (e) 2 months  | 1.8mm
| (f) 7 years   | 4mm
of foetal development, several generations of saccules appear from each terminal duct. These terminal sacks are so short they have an irregular appearance, not displaying the regular cup-shaped geometry of alveoli, although they do have a blood-gas barrier the same thickness as found in the adult and so are capable of gas-exchange (81).

1.4 Alveolar Development

At birth the acinus is approximately 1.1mm in length and generally consists of three respiratory bronchioles, a transitional duct leading to three saccules ending in terminal saccules (15). The actual numbers of each element in the acini may alter in different axial pathways but the development and differentiation continues to give an average acinar length of 4mm at 7 years of age when the branching development is complete. From birth to adulthood the greatest contribution to the increase in the gas-exchanging surface area is the development of the alveoli. There is considerable debate over the number of alveoli present at a given time. This is most likely a reflection of the technical difficulties involved in alveolar counting (154). At birth the number present has been reported to vary from zero (127) to the full adult complement (111). The consensus of opinion, however, seems to indicate a number approaching 30 million but these are likely to be primitive terminal air sacks as the first mature alveoli do not appear until some five weeks later (128). Since the number of alveoli in adulthood is reported to be about 300 million (2) there must be a tenfold increase in the number from birth. Considerable alveolar multiplication occurs, the greatest rate of which is in early post-natal life, before 4 years (128).

The mode of alveolar formation has been studied in relation to the elastic tissue organisation; this has been cited to be responsible for the development of new alveoli (56). Elastic tissue stabilises the alveolar wall and at birth is consolidated around the mouths of the alveolar ducts. There are reported to be three methods of alveoli formation:
segmentation, compoundment and alveolarisation (Fig 1.2). Segmentation involves the division of the primary alveolus (the most distal unit) into smaller segments which subsequently develop into mature alveoli. This division is brought about by the protrusion of the alveolar wall between bundles of elastic tissue gathered around the perimeter of the primary alveolus. Due to the pattern of the elastic tissue organisation this has been termed the 'fish-net' theory. Compoundment is very similar to segmentation except that the elastic tissue bundles collect in the alveolar septae. In this way new alveoli are formed laterally with respect to the alveolar duct. Alveolarisation is the process by which alveoli develop in the walls of previously non-alveolated airways. Similar to canalisation this occurs in a centripetal fashion so that previously conducting airways are converted to respiratory bronchioles (16). Thus terminal bronchioles become incorporated into the acini from which there is a diminution in the number of such airways during infancy (17). It is likely that conversion of terminal bronchioles to respiratory bronchioles occurs late in infancy after the conversion of respiratory bronchioles to alveolar ducts due to the centripetal nature of the process (13).

With respect to the increase in the surface area of the gas-exchanging region of the lung, alveolarisation is less important than segmentation although all three methods will contribute to the increase in surface area from $6.47 \text{m}^2$ at three months to $75 \text{m}^2$ in the adult (53). There is some controversy over the age at which this hyperplastic growth of the alveoli ceases (127, 154). Many consider the adult number to be reached by 8 years of age; thereafter growth is considered to be solely hypertrophic with an increase in the size rather than the number of existing units. Others (154), however, have commented on the wide variation in the number of alveoli in the adult lung (range 200-600 million) and cases have been cited where values within the adult range have been found as early as 48 months (53). This fact and the obvious lack of longitudinal data available tend to
Series 2, 3 and 4 illustrate 'segmentation';
Series 5, 6 and 7 illustrate 'compoundment'
and 8 and 9 illustrate 'alveolarisation of terminal bronchioles'

(From: Emery, J.L. (1970)(55))
infer that alveolar multiplication after the age of 8 years is possible. It may even occur into adulthood although most probably ceases before somatic growth stops (154).

Even if alveolar multiplication continues throughout growth it is not solely responsible for the 28-fold increase in lung volume from 200ml to 5.5 litres at 25 years of age (53). Lung volume increases at a greater rate than can be accounted for by the increase in the number of alveoli. Clearly, the alveoli must enlarge. Alveolar diameter increases from 40-120μ at birth to 250μ in the adult (164). The average interalveolar distance (alveolar intercept : Lm) increases by a third (155). This is a smaller rate of increase than that for alveolar size as it is a function of both alveolar size and alveolated airway diameter. Unlike alveolar volume (Vₘ), Lm is independent of body size and lung volume. Nevertheless, since the most rapid increase in alveolar size is reported after 10 years of age (55) the deduction that alveolar multiplication is succeeded by proliferation of existing units seems probable. However, alveolar multiplication contributes more to the increase in lung volume than does actual enlargement of the alveoli (155).

1.5 Vascular Development

The growth and development of the pulmonary circulation parallels that of the tracheobronchial tree and alveoli. The pre-acinar vessels follow the developmental pattern displayed by the airways. The intra-acinar vessels follow the developmental pattern of the alveoli (129). In the adult there are two blood circulations supplying the lungs. The bronchial circulation carries oxygenated blood to the conducting airways, pulmonary blood vessels, perihilar visceral pleura, pulmonary nerves and ganglia, lymphatic and connective tissue. The pulmonary circulation carries deoxygenated blood to supply the acini and portions of the pleura. The two circulations communicate through anastomoses found proximal to the terminal bronchioles. There are reportedly two types of anastomic connections 0.05-0.5mm in diameter and 0.1-10mm in length (122). Both allow the bronchial
circulation to sustain portions of the lung parenchyma when the pulmonary arteries are occluded. This reserve mechanism brings oxygenated blood to specific areas of ischaemic lung tissue. The bronchial system is smaller in comparison to the pulmonary system; most of the lung structure drains into the pulmonary veins even those supplied by the bronchial artery. The only true bronchial veins drain from the hilum to the azygous or systemic system (83).

1.5.1 Pulmonary Circulation

The pulmonary circulation is the major circulation in the lung and the first to appear in the foetus. The lung, similar to any developing organ, has a plexus of blood vessels before it is linked to the rest of the body circulation. In the embryonic period the pulmonary arterial trunk develops from the 6th bronchial arch. By the 7th week of gestation the mature pattern of linkage between the heart and lungs is complete and there is a patent ductus arteriosus (83). Before this, the vessels drain into the systemic system of the foregut and trachea. During the pseudoglandular period the pulmonary arteries develop along with the airways of the tracheobronchial tree closely following their branching pattern. There are two types of pulmonary artery, conventional and supernumerary. Conventional arteries accompany the developing airways and branch with them. Supernumerary arteries, on the other hand, do not accompany the airways but emerge from the conventional arteries at right angles and supply the alveolar region around the airway and intra-acinar region. These are smaller and more numerous than conventional arteries, particularly in the periphery where they outnumber the conventional arteries approximately 3:1 (83). At the end of the pseudoglandular period (16th-17th week of gestation) all the pre-acinar arteries are formed as the branching of the pre-acinar airways is also complete at this time. There are more pre-acinar arteries than airways as supernumerary vessels have developed although there are no detectable alveoli.
The pulmonary veins develop after the arteries (80), they are visible at two months gestation but the completion of all the pre-acinar veins does not occur until late in the cannicular period (83). At this time there is little blood flow through the pulmonary circulation. This suggests that the branching development is not dependent on the blood volume or flow. The pulmonary veins are found in the pleura and connective tissue septa. Their pathways are independent of the airways and arteries at the periphery of the acinus and they have their own connective tissue sheath. The aetiology of the pulmonary vasculature branching pattern may be genetic. It has been demonstrated that the pattern displayed by monozygotic twins is closer in comparison to that displayed by dizygotic twins (78), although this relationship has not been found with respect to the bronchial tree pattern of branching.

1.5.2 Bronchial Circulation

The bronchial circulation forms a secondary system in the human lung. The bronchial arteries arise from the aorta and intercostal arteries in the 9-12th week of gestation (15); that is before the bronchial tree branching is complete but after the appearance of the pulmonary arteries (129). At the hilum, bronchial arterial branches go to the oesophagus and mediastinal pleura, but in the lung they develop along the bronchi supplying the airways and their accompanying vessels. The bronchial arteries eventually divide into broncho-pulmonary branches which form capillary networks to supply portions of the lung parenchyma. These networks are similar to the pulmonary capillary networks in diameter but are distinguished by their irregular pattern. The most distal areas of the lung are supplied exclusively by the pulmonary artery as the bronchopulmonary branches of the bronchial artery are not found for several generations proximal to the terminal bronchiole. In general the bronchial arterial development may be considered to parallel the formation of the cartilage in the bronchial tree (122).
1.5.3 Vascularisation of Acinus

In the cannicular period the process of canalisation occurs which involves the vascularisation of the acinar region of the lung. This corresponds to the period when the acinar airways are rapidly developing and the two processes in conjunction ensure that the acini are capable of gas-exchange at birth. As the most distal airways grow and divide they are matched in their pattern of branching by the conventional arteries which follow the intra-acinar airways closely. Supernumerary arteries branch into the acinar tissue and form capillary networks which invade the lung parenchyma and alveolar wall to create the blood-gas interface (78).

In the terminal sac period this distal growth of the pulmonary vasculature continues. Both conventional and supernumerary arteries appear in the acinar region; the former being more numerous. As both types of artery increase in length and diameter there is a relatively greater increase in the size of the conventional arteries. Existing pre-acinar arteries increase in size but not in number and the rate of dimensional growth is similar after birth in conventional and supernumerary vessels.

1.5.4 Postnatal Development

At birth the pulmonary circulation changes from a high resistance system to one of low resistance as blood flow through the vessels increases rapidly (154). In the foetus normally only 10% of the combined ventricular output passes to the lung circulation. The remainder passes through the ductus arteriosus to the aorta due to the high resistance in the pulmonary arteries. The foramen ovale contributes to this pulmonary bypass by allowing interatrial passage of blood. At birth, with the onset of air breathing, blood flow increases as the pulmonary resistance falls. This is due to the increase in oxygen tension causing widespread dilatation and, in part, to the unwinding of previously coiled capillaries (83). The post-natal fall in the
pulmonary resistance lowers the pulmonary arterial pressure to about half that of the systemic pressure in three days; the adult value is reached by 6 months of age. The ductus arteriosus closes by constriction at 2 months; the foramen ovale at birth (83).

Post-natal development of the pulmonary vasculature is closely associated with the growth changes occurring in the bronchial tree. Immediately after birth there is a rapid increase in the number of pre-acinar arteries. This reflects the period of alveolar multiplication and consequently there is a relatively greater increase in the number of supernumerary arteries which supply them. The ratio of supernumerary to conventional arteries increases until about 5 years of age, when the adult intra-acinar value is reached (79). The number of alveoli per artery decreases in this period suggesting that alveolar multiplication precedes arterial development in early post-natal life (154). As the emphasis of alveolar development alters from hyperplastic to hypertrophic growth so the pulmonary arteries are seen to increase in size rather than number. Indeed, the number of small vessels per cm$^2$ of lung tissue decreases after the period of rapid alveolar multiplication. This is due to the rise in the number of larger arteries (100-200$\mu$m) as a result of increasing arterial size and to the increasing size of the alveoli resulting in the separation of the arteries (83). There is a change in the thickness and structure of the arterial wall after parturition (Fig 1.3). In the foetus, for a given sized artery, the arterial wall is twice the thickness of that found in the adult (88). Due to the physiological changes at birth, the increased oxygen tension, vasodilation and decreased pulmonary resistance, the wall thickness decreases and, by about 18 months, the ratio of wall thickness to external diameter has reached the adult value of 1.4% (45). As the arteries increase in size there is a lag in the development of their muscular walls. It may appear that the muscle tissue "recedes" into the larger arteries as the infant develops. This is not due to
FIG. 1.3 DEVELOPMENT OF MUSCLE IN PULMONARY ARTERIES WITHIN THE ACINUS WITH AGE

TB = terminal bronchiole  RB = respiratory bronchiole
AD = alveolar duct       Alv. = alveolus

(From: Reid, L.M. (1979)(129))
atrophy of the arterial muscle but the growth in the arterial size with no new muscle formation (45). Post-natal development, therefore, involves the remodelling of the arterial wall so that muscle continues to extend toward the periphery until early adulthood.

1.6 Nervous Tissue Development

In order for the major lung structures to function efficiently the lung is innervated by nervous tissue. Movement of the thorax and diaphragm may inflate and deflate the lung but the influence of the intrinsic nervous tissue provides the regulation necessary for respiratory function. Relatively little is known of the mechanisms involved in the nervous system regulation within the lung itself, much less about its growth and development to adulthood. One of the reasons for this lack of information is the inherent difficulties associated with assessing a multi-component system. It is one thing to measure a nervous reflex quantitatively and discuss the pathway involved but quite another to quantify that reflex action where it may be masked or modified by secondary changes not under specific investigation. Thus the investigation of lung nervous tissue has been hampered by its complexity and the attention necessarily given to the specific elements of the system rather than the system in general.

The adult human lung is supplied by branches of the vagus and phrenic nerves. There are two types of nervous tissue in the lung: efferent (vegetative, motor) and afferent (visceral, sensory). The efferent fibres include both parasympathetic and sympathetic elements; the preganglionic fibres are myelinated, the postganglionic are non-myelinated. They become fine nerve fibrils distributed in the bronchi, pulmonary parenchyma, blood vessels, musculature and pleura. The afferent nerve fibres are large myelinated nerve fibres which arise from sensory receptors in the bronchi, blood vessels, parenchyma and pleura which participate in reflexes which alter the respiratory function in a range of different environments (108).
1.6.1 Receptors

There are several types of sensory receptors in the lung which regulate breathing; three receptors are of particular importance.

Pulmonary stretch receptors lie in the smooth muscle of the intrapulmonary conducting airways. They are stimulated by changes in the calibre of the airways and are supplied by fast conducting myelinated fibres. They slowly adapt and when they are stimulated by inflation of the lungs the central action of the respiratory rhythm generator is to inhibit inspiration. It has been shown that they do not produce this reflex during normal breathing in man but require larger inflations than tidal volume to respond (> 800ml) (36). Their main role is to adjust the pattern of breathing (rate and depth).

The irritant receptors are subepithelial mechano-receptors located in the trachea, bronchi and bronchioles. They are also present in the nose, larynx and pharynx. They ramify between the epithelial cells and extend as far as the ciliary layer to detect deformation of the epithelial surface. The small diameter myelinated fibres in the vagus have a conducting velocity of 12.9m.s\(^{-1}\) and the receptors adapt quickly which makes them quite distinguishable from pulmonary stretch receptors (165). The irritant receptors respond to various stimuli (dust, gaseous irritants, and probing), and these cause reflex bronchoconstriction. The cough reflex is not usually initiated unless irritant gases and intraluminal catheters are introduced into the lungs.

Type J pulmonary receptors (juxtacapillary) were so called due to their probable location close to the alveolar capillary barrier but there is no histological evidence to support this theory (165). They respond to pulmonary capillary congestion, capillary hypertension and oedema of the alveolar wall by causing rapid shallow breathing, hypotension and brachycardia. They are difficult to study as the unmyelinated C-fibres are very fine and difficult to
dissect. They could be part of a 'nociceptive' or 'protective' afferent system in the lungs (165).

In the hilum both efferent and afferent nervous tissue is present in the anterior and posterior nerve plexuses. They are distributed in the lung as mixed fibre bundles that follow the branching pattern of the bronchi and blood vessels forming extra- and intra-chondrial plexuses. The bronchial pathway contains many multipolar ganglia each with 2-10 ganglion cells mainly accompanying the large bronchi becoming less frequent as they extend distally. The pulmonary arteries show a greater amount of innervation than the corresponding veins throughout the pulmonary vasculature. Only occasionally are ganglia exhibited which, like the bronchial pathway, are primarily located at branching points. This general description of pulmonary nervous tissue has been established for the neonate (8 months old) and is the accepted pattern seen in the adult (165).

1.6.2 Embryological Development

General nervous tissue derives from neuroectoderm with the formation of the neural tube and neural crest early in the embryonic period. The neural tube undergoes many specialisations to become the brain and spinal chord. The neural crest develops into a collection of nerve cells located outside the central nervous system that will participate in the formation of the more peripheral parts of the nervous system. Neuroblasts from the neural crest migrate through the mesenchyme to form the extrapulmonary nerve plexuses at the hilum, from which the lung derives its nervous tissue. Necessarily this occurs before the separation of the trachea and oesophagus at five weeks of gestation. The intrapulmonary parasympathetic ganglion cells found accompanying the pulmonary bronchial and vascular systems are formed later by the propagation of these pioneering neuroblasts. The general growth of nervous tissue has been linked to the ground substance in which it develops (102). In the lung, this constitutes the
mesenchyme from which connective tissue elements derive and it is indeed through the network of these elements that the developing axon advances to make contact with the appropriate receptors. What chemical or physical force controls this growth is unknown but the presence of the connective tissue ground substance is an important factor.

The growth of the nerves chronologically follows the development of the tracheobronchial tree and vascular systems. The nervous tissue innervating the tracheobronchial tree develops more rapidly and precedes the innervation of the pulmonary vasculature (153). At the beginning of the pseudoglandular period (7th week of gestation) ganglion cells are present in the extrachondrial tissue of the trachea and extend to the second order bronchi. This tissue divides equally at the carina to supply the right and left bronchi. As there is progressively less smooth muscle in the developing segmental bronchi there is relatively less intrachondrial nervous tissue in the bronchial tree. At this time the extrapulmonary arteries and veins are well supplied with nerves but there is no apparent intrapulmonary vasculature innervation, illustrating the delay in the development of the pulmonary circulation nervous tissue (153).

At the beginning of the cannicular period all but the smallest bronchioles have an extrachondrial plexus of nerves; toward the periphery the extra- and intra-chondrial plexuses fuse. Meanwhile the pulmonary vascular innervation extends toward the periphery with growth; the foetal intrapulmonary arteries being more richly supplied with nerves than the intrapulmonary veins (102). Myelinisation begins in the cannicular period occurring proximally in the oldest part of the nervous system first; by the end of the terminal sac period the nerves entering the lung are well developed. The terminal sac period is the final stage of foetal development when the nervous system innervates the muscular coat of the pulmonary vasculature and nerve fibrils, generally multipolar, send branches from the submucous nerve plexus which terminate in the smooth muscle
and intraepithelial spaces. In the neonate of 8 months the adult pattern of nerve supply is established (102). The pulmonary vascular nerves extend with fine fibrils forming a plexus as far as the arterioles. These mingle freely with the fibres from the peribronchial nerves but do not extend to the alveolar walls. In the parenchyme filaments follow the course of the capillaries in the alveolar duct and air sacs and end in relation to the capillary walls. These fibres are widespread throughout the lungs. Thus nervous tissue development and growth involves migration, elongation and differentiation. It most probably continues to grow in size and complexity for several years through to adulthood.

1.7 Connective Tissue Development

The predominant structures of the lung are the airways, alveoli and pulmonary vasculature but the bulk of the lung tissue consists of connective tissue (64). This tissue surrounds and supports these structures and is intimately linked with their function and growth. Lung weight increases from 60g at birth to 700g in the adult (88). This may be attributed to the air trapped within the tissue and to the proliferation of lung tissue including airway mucosa, alveolar walls, intra-alveolar septa and a portion of the pulmonary blood supply. There is no difference in this growth pattern between either the right or left lungs or their individual lobes (163). The specific gravity or density of the lung decreases and there appears to be no direct relationship between lung parenchymal tissue growth and functional airway size (88). The contribution of connective tissue proliferation to the increase in lung weight during growth is probably considerable (143) but it is only recently that the biochemical analysis of such a complex microscopic structure has become available. Indeed the technical difficulties of analysing the individual elements of connective tissue have hindered the categorisation and quantification of the structures involved. Another difficulty is the lack of human data available; most data rely on other species and it is difficult to extrapolate these findings to man.
The connective tissue of the lung is found in the lung parenchyma, pleurae, septae and alveolar interstitium. Its constituents are found within the airways, alveoli and pulmonary vasculature. Connective tissue involves the widespread intrusion of cellular components throughout the entire respiratory system. There are three main categories of connective tissue: collagen, elastic fibres and proteoglycans (73). (Reticulin fibres may be considered to be mostly collagen in constitution). These are the most abundant as assessed biochemically, although there are over forty different cell types in the lung parenchyma. There are two major proteins associated with connective tissue. Collagen and elastin, incorporated in a ground substance chiefly of acid mucopolysaccharides of which proteoglycans are a main feature.

1.7.1 Collagen

Collagen is the most abundant protein in the connective tissue as it constitutes 60-70% of the total connective tissue mass, which represents 10-15% of the dry weight of the adult lung (41). A total of 30-40% of lung collagen is found in the large airways, large blood vessels and the septa dividing the major lung segments. In the tracheobronchial tree it is found as part of the cartilaginous system which extends up to the 9th generation and is involved in the structure of the vascular tree and pleura. There are three recognisable forms of collagen: basement membrane, microfibrils and fibrils. Of these the collagen fibril is the unit of collagen thought to determine its mechanical properties (73). The fundamental unit of collagen is the tropocollagen molecule formed intracellularly from the precursor proprocollagen. Synthesis of collagen begins on the polyribosomes attached to the endoplasmic reticulum and the final association of tropocollagen, with its three alpha chains, into collagen fibrils occurs extracellularly. There are five known alpha chains, each with a different sequence of amino acids, and four known types of tropocollagen. Collagen tissue is heterogeneous, that is each lung structure is associated with a specific type of collagen. Collagen synthesis is first seen in the lung during the pseudoglandular period,
before the 16th week of gestation, and many cells are capable of synthesis notably the fibroblasts, smooth muscle cells and endothelial cells (59). In the foetus 3-4% of the total protein synthesis is attributed to collagen and at birth collagen is the principal connective tissue around the air passages, blood vessels, pleura and septa but not in the alveolar walls. After birth, in the first month, there is a shift in the emphasis of protein synthesis toward collagen. The total amount of collagen in the lung increases fivefold as 14% of amino acids that produce protein in the lung go towards collagen synthesis (41). This increase in the rate of collagen synthesis disappears at 2-3 months of age as the level returns to 3% which is the adult value. The ability of the lung to alter protein synthesis whenever the lung grows indicates that collagen may be increased whenever there is rapid lung growth. (73).

1.7.2 Elastic Fibres

Elastic fibres consist of the protein elastin in association with microfibrils (59). Little is known about the microfibril except that it contains no hydroxylysine proving that no type of collagen is involved. Elastin is not the only protein constituent of elastic fibres but it is the presence of elastin that presumably gives these fibres their rubber-like qualities. If put under high tension in the laboratory they are capable of stretching to several times their length and when released they return to their original size and shape; this shows high distensibility and low tensile strength.

The precursor of elastin is tropoelastin which is synthesised on the rough endoplasmic reticulum of mesenchymal cells (73). It is thought that two cell types are responsible for synthesis, fibroblasts and smooth muscle cells, although chemically it appears that the latter are more important. Elastic fibres are not apparent until the 24th week of gestation, this is later than collagen but there are more technical difficulties in assessing the presence of elastin. By three months gestation pleura,
blood vessels, bronchi and respiratory units all contain elastic tissue but this is incomplete at birth. Elastic fibres are found primarily in the alveolar interstitium and are absent in the parietal pleura (101). There is no significant change in elastin from 19-40 weeks of foetal age although there is probably a decrease in the percentage of microfibrils with development, so that the elastic properties of the fibres increases. The synthesis of elastin and the production of elastic fibres does not show the burst of activity displayed by the collagen synthesis just after birth.

During growth the total elastin content of the lung increases while the collagen content remains constant (105, 157, 167). This increase in elastin, however, occurs in the inter-lobar septa, pleura and perhaps the bronchi and vessels whereas the ratio of elastin and collagen in the terminal air spaces remains the same at all ages. Indeed, as collagen is twice as abundant in the respiratory bronchioles and alveolar ducts and shares a close helical association with elastin in this region it may prove as important a protein as elastin, if not more so, in the development of lung elasticity.

1.8 Summary

The development of the pulmonary system follows a definite pattern, although the timing of these phases of growth may be in dispute. Nevertheless, three biological processes have been proposed to describe the major events of lung development (83):-

1) The bronchial tree is developed by the sixteenth week of intra-uterine life (26).

2) Alveoli rapidly develop after birth by multiplication, which is superceded by hypertrophic growth until growth of the chest wall is complete in adulthood (45, 53).

3) The pre-acinar vessels (arteries and veins) follow the development of the airways; the intra-acinar vessels follow the development of the alveoli. Muscularisation of the
intra-acinar arteries does not keep pace with the appearance of new arteries (79, 80).
CHAPTER 2

FUNCTIONAL DEVELOPMENT OF THE LUNG
2.1 Introduction

In the previous chapter the anatomical development of the respiratory system was described. The growth of the lung was illustrated using anatomical evidence from the foetus to the adult and the pattern of growth of the major features of the lung was discussed. In this way an overview of the development of the respiratory system has been given.

The purpose of this chapter is to extend this view to include those indices of lung function which reflect the underlying physiological development; this in turn parallels the pattern of growth already described.

Measurements which describe aspects of the lung’s function have been available for some time. These range from simple volumetric indices to complex techniques and equations. They are used primarily to determine the ‘normality’ of the respiratory system. A change in lung function indices over time is usually associated with the process of ageing or disease. However, growth and development of the lung is reflected by lung function indices up to the time when the lung deteriorates with age in the adult. The cessation of lung growth probably occurs in the age group 18-25 years but the exact timing is debatable.

During the initial period of lung growth the indices of lung function are difficult to measure consistently. Up to the age of 6 years the child finds it difficult to perform the manoeuvres required. Some lung function indices are effort dependent and thus almost impossible to obtain. Lung function indices often have to be extrapolated or interpolated to illustrate growth. This causes obvious difficulties when interpreting such data and it is unfortunate that this coincides with the time when the lung expands so rapidly. It is a truly prolific stage of lung development; the lung volume increases sixteenfold up to the age of 6 years and thence only threefold to the adult value. In the neonate, lung function indices are somewhat easier to measure. The act of crying is said to be at the limit of the respiratory systems’ capabilities. As such it is used to measure the indices of forced expiration without needing the co-operation of the
child. However, as with all lung function testing at any age, the introduction of external apparatus may alter the intrinsic nature of the system. This may be of particular importance in the neonate.

After the age of 6 years, lung function indices can be measured easily and consequently there is a wealth of data up to and including adulthood. The data which have been collected during this period of lung growth are primarily from cross-sectional studies. These may not be the best studies from which to determine patterns of lung development. Cross-sectional studies may mask the underlying changes occurring over time (65). The most accurate interpretations of growth patterns are assessed using data from longitudinal studies. However, these are more difficult to conduct and consequently there are less data available from longitudinal studies.

2.2 Anthropometry

Growth of the lung parallels the overall body growth occurring from childhood to adult (93). As the bones elongate, muscles develop and the internal organs grow and expand in the available space. The extent of this somatic growth is easily determined using anthropometric measurements of external body dimensions. The most important measurement is that of stature. The height of a child is closely related to the development of the tissues. It is a better indicator of the stage of development than chronological age (48). Thus growth is not a function of age per se. This may not be surprising as children of the same age show wide variations in their heights and individual functional development. As height is such an important index it is the most commonly recorded anthropometric measurement but other variables may reflect the growth of the underlying tissues more accurately. The length of the thorax is a subdivision of the measurement of height. However, it may be more closely associated with lung growth as the lungs are contained and develop within the thorax. Certainly the anteroposterior and transthoracic dimensions increase with growth. This must reflect the underlying development of the respiratory structures. The chest width is thought to be particularly associated with lung growth (29).
Since height is such a good predictor of growth the lung grows in proportion to the change in height over time. The expression of height in formulae, usually incorporated as height cubed for children and height squared for adults, has been used to predict lung function indices (120). However, the lung is unlikely to develop according to precise symmetry and simple geometric formulae may not apply during the years of growth. It is also incorrect to assume that during the period of somatic growth all the anthropometric indices increase with relation to individual tissue development. For instance, body weight increases but not in proportion to the growth shown by some internal organs. In the case of the lung, the increase in body weight initially reflects the increase in lung function. This has been termed the muscularity effect (132). However, if the weight continues to increase it may be mirrored by a decrease in lung function due to obesity. This is an example of a physiological paradox which can occur with growth.

2.3 Chest Wall and Maximal Respiratory Pressures

The outward dimensions of the chest not only reflect internal organs but also the change and development of the respiratory structures of the rib cage and chest wall. At birth the chest wall is highly compliant but it gradually becomes more rigid. This is necessary to help maintain the interdependence between lung units and has the mechanical advantage of increasing local pleural pressure over lagging segments of the lung. The decrease in chest wall compliance occurs immediately in the post-natal period due to changes in the tissue characteristics of the rib cage. Consequently, there is a decrease in total respiratory compliance from birth to adulthood. During growth there is an increase in the outward recoil of the chest wall which may be due to changes in the mechanical properties of the rib cage. It may also be due to the disproportionate growth of the chest wall relative to that of the lung. The latter is a predominant feature in the upright child possibly due to the growth of the abdomen and the consequential effect on sub-diaphragmatic pressure. The abdomen acts as a fluid filled container with a flexible anterior abdominal wall. Due to gravity, the pressure in the upper part of the abdomen is negative; the lower part
being more positive (the abdominal hydrostatic column). The negative pressure on the abdominal surface of the diaphragm in the upright position reduces the outward recoil of the chest wall. As the abdomen grows and increases in length so the abdominal surface of the diaphragm becomes more negative. Thus the change in the recoil of the chest wall may be due to both the growth of the abdomen and to gravity.

The respiratory muscles, which are an integral part of the chest wall and rib cage, also develop during the period of growth. There is an increase in muscle strength with age; the shape of the thorax in children compensates for their weaker muscles (24). There is also evidence of sex differences, in that boys are much stronger than girls (159). Respiratory muscle strength can be reflected by the measurement of maximal pressures generated by the respiratory system. Usually these are taken at total lung capacity (TLC) which is itself a measure of lung size and development. The maximal respiratory pressure increases with age as a result of increased muscle strength. However, the lung size is also increasing so that the increase in lung volume may account for some of this increase in maximal respiratory pressures (24). Therefore, the increase in TLC, reflecting lung growth, is a result of both an increase in lung tissue volume and the increasing strength of the child. This is important when relating lung growth indices to measurements of TLC. The strength of the respiratory muscles may be increased by factors other than muscle growth. The level of habitual activity and life at high altitude will increase the size and function of the lung by increasing muscle strength through, respectively, training and acclimatisation (117). This has to be taken into consideration when interpreting values for individual children. It has been suggested that, to circumvent these problems of differing muscle strengths, the volume at a fixed distending pressure be used instead of TLC (2.45kPa) (104).

2.4 Lung Volumes

Discussion of the development of the chest wall and rib cage leads inevitably to discussion of the growth and development of the lung itself. The lung develops within the thorax and can be
crudely monitored by measuring lung widths and lengths from chest X-rays. These reflect the overall growth of the organ but are very variable and consequently a poor substitute for direct measurements of TLC (140). By far the best indication of lung growth is given by functional indices which reflect the changes in the internal structures of the lung. Lung size is reflected by the amount of air that is contained within the developing airways and alveoli. This volume, the total lung capacity (TLC), and its subdivisions increase with lung growth (Fig 2.1). Similarly, indices which are also dependent on the development of the airways and alveoli such as FEV₁ (forced expiratory volume in one second) and T₁ (transfer factor) are also determined by the size of the lung.

The volume of the lung may be divided into that contained within the conducting airways (VDS) and the remainder from the gas-exchanging portion of the lung (VT - VDS), the alveolar volume (VA). The tidal volume (VT) has been reported to have a relationship to body weight from birth to adult (7-10 ml·kg⁻¹) and the ratio of ventilatory dead space to tidal volume (VDS/VT) also remains largely unaltered (1:3) throughout development (50). However, due to the increased metabolic needs of the small infant and the small gas-exchanging surface area to lung volume, the respiratory rate is 34-36 breaths per minute at birth compared to 12-16 in the adult (109). Nevertheless the useful part of the breath (VT - VDS/FRC) is identical in the neonate and the adult, proving that the growth patterns of resting lung volume, tidal volume, dead space volume and minute ventilation are well co-ordinated throughout growth (Fig 2.2).

2.4.1 Conducting Airways

The development of the conducting airways contributes to the increase in lung volume associated with growth. There is some debate whether this growth is dysanaptic or isotropic (68, 88, 169). Anatomical studies suggest that proximal airways grow relatively faster than distal airways in early post-natal life (42); the relationship, which depends on age, supports the concept of dysanaptic growth. Isotropic or equidimensional growth theories, based on physiological
FIG. 2.1 LUNG VOLUMES

Total lung capacity and its subdivisions

<table>
<thead>
<tr>
<th>Volume of air in lungs (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6000</td>
</tr>
<tr>
<td>2900</td>
</tr>
<tr>
<td>2400</td>
</tr>
<tr>
<td>1200</td>
</tr>
</tbody>
</table>

IRV  Inspiratory reserve volume
TV   Tidal volume
ERV  Expiratory reserve volume
RV   Residual volume
IC   Inspiratory capacity
FRC  Functional residual capacity
VC   Vital capacity
TLC  Total lung capacity
FIG. 2.2 LUNG VOLUMES IN THE INFANT AND ADULT

(From: Nelson, N.A. (1976)(109))
data involving airway resistance (169) have been severely
criticised. Their assumption that the tracheobronchial tree
exhibits total laminar flow is widely refuted (105). Since
these theories are based fundamentally on this assumption
such criticism is justifiable. This lends further credence
to the theory that growth is dysanaptic. (20, 28, 68, 105,
156).

The peripheral or small airways of the conducting system
contribute more to lung volume than the central airways. In
the age group 7-20 years there is a twofold increase in the
anatomical dead space (V_D) whereas the functional residual
capacity (FRC) increases threefold (75). A change in the
dimensions of the small airways can have a marked effect on
volume. This is due to the relatively greater number of
these small airways and consequently to the large
cross-sectional area they maintain. The development of the
peripheral airways is an important aspect of lung
maturation. Generally in children, the size-related lung
function indices are similar in proportion to those found in
early adulthood before the onset of decline due to ageing
(37). However, this is not true of the indices that reflect
the calibre of the most distal airways. The conductance and
stability of these small airways are related to the
gas-exchanging properties of the lung and to the expiratory
flow limitation. In young children the limitation to
expiratory flow is initially airway closure due to the
dynamic compression of the smaller airways (144). This can
be measured as the closing volume (CV) which, when added to
residual volume (RV), gives a value for closing capacity
(CC). As the child grows the chest wall becomes more rigid.
The closing volume decreases and the closing capacity falls
as the residual volume is limited by the chest wall. In the
young adult the closing volume is not detectable as the
dependent small airways do not close above residual volume
(104). With increasing age in the adult the closing volume
(and thus closing capacity) increases until airway closure
is large enough once again to limit the expiratory flow
above residual volume. It is, therefore, apparent that a 7
A year old child will have a CC (expressed as %VC) similar to that of a 45 year old adult.

The dimensions of the small airways can also be shown to have an effect on the frictional resistance to expiratory airflow in this region of the lung. The maximal expiratory flow volume curve (MEFV) introduced by Hyatt and Osley has a characteristic shape towards the lower lung volumes (Fig 2.3)(99). This shape is independent of effort and reflects the integrity of the smaller airways as they empty. In the young child the MEFV curve shows convexity to the volume axis as frictional resistance to the laminar flow in the small airways dominates the emptying rate (Fig 2.3). In teenagers and young adults the MEFV curve is concave to the volume axis over almost all of the vital capacity (VC). This is due to the increase in the lung elastic recoil which diminishes the importance of frictional resistance in the smaller airways. However, throughout adulthood there is a loss of elastic recoil and the frictional resistance in the smaller airways dominates at increasingly high lung volumes so that the MEFV curve once again becomes convex to the volume axis (Fig 2.3). In spite of these obvious changes in the shape of the MEFV curve with growth and ageing it is difficult to use the values of expiratory flow at the lower lung volumes to reflect the change occurring in the small airways. The flow rates at 50%VC ($V_{50}$) and 75%VC ($V_{75}$) are variable; it is difficult therefore to make comparisons between individuals (99).

2.4.2. Acini

Development of the conducting airways is followed by development of the gas-exchanging portion of the lung. The alveolar surface increases markedly from birth so that the average alveolar surface area at TLC is 6.5m$^2$ at 3 months, 32m$^2$ at 8 years and 75m$^2$ in the adult and, from the point of view of ventilatory function, the alveolar surface area is more important anatomically than functional residual capacity (FRC) (53). This growth is proportional to age and height but not to body surface area. Similarly, the overall
FIG. 2.3 MAXIMUM EXPIRATORY FLOW VOLUME CURVE (MEFV)
A-D represent typical curves at various ages

(From: Boyden, E.A. (1977)(17))
lung volume correlates closely with height (in the manner of $Ht^2$ or $Ht^3$) but not with body weight. Indeed there is a more rapid growth in lung volume in the first 3 years of life than would be expected from backward extrapolation of height related adult values (92). This may be due to the early rapid development of alveoli at birth. In the early age group (< 1 year) the alveolar surface area increases at a faster rate than can be accounted for by the corresponding increase in lung volume. Later the growth in lung volume increases according to the relationship of $Ht^3$ (or $Ht^2$). There is an obvious cause and effect relationship between the growth patterns of alveolar number and size. At first the alveolar number increases rapidly; it then remains constant before increasing again slowly. Alveolar size also increases but linearly to cross the numerical growth curve in early adolescence (82). A similar growth relationship is found with alveolar surface area and lung volume.

2.5 Lung and Chest Wall Elasticity

The volume of air in the lung is an indication of lung size and, therefore, lung growth. It is a measure of the air contained within the conducting airways and the gas-exchanging portion of the lung. The intrinsic growth of these airways and alveoli themselves are not the only factors which affect the measurement of lung volume. Total lung capacity (TLC) and the proportions of its subdivisions (Fig 2.1) also depend on the mechanical balance between the elastic forces of the lung and thorax. These elastic forces can be measured and are expressed in terms of the elastic recoil of the lung and chest wall. The elastic recoil of the lung can be measured at varying lung volumes. An oesophageal balloon is used to determine oesophageal pressure which reflects pleural pressure. By interpreting pleural pressure with respect to intra-alveolar pressure the elastic recoil across the lung (transpulmonary pressure) at a given lung volume can be obtained. This measurement ($P_{st}$) is directly related to the elastic forces operating in the lung tissue and can change as a result of a change in the pulmonary elasticity (74, 170). The greater the amount of elastic recoil in the lung ($P_{st}$) the smaller the total lung capacity (TLC) or vital capacity (VC) but the larger
the ratio of forced expiratory volume to vital capacity (FEV₁/FVC). This is due to the elastic recoil increasing airway calibre by holding the airways open and, therefore, allowing the lung to empty more rapidly.

The measurement of \( P_{(st)} \) should not be confused with the measurement of lung compliance which can be obtained at static volumes \( (C_{1}) \) or continuously during a single (dynamic) manoeuvre \( (C_{dyn}) \). Lung compliance is a measure of the distensibility of the lung and is influenced by the elastic recoil. To this extent \( P_{(st)} \) is closely related to the measurement of lung compliance, in particular to that of \( C_{1} \) (74).

The elasticity of the chest wall is far more difficult to determine. Usually it is obtained during anaesthesia or when there is muscle paralysis. The development of the chest wall has been discussed earlier. To reiterate, the mature foetus has an almost infinitely compliant chest wall above FRC. As the child develops the distensibility of the chest wall decreases and becomes increasingly rigid.

2.5.1 **Elasticity Changes with Growth**

The elasticity of the lung increases with growth as elastic recoil \( (P_{(st)}) \) increases throughout childhood. Up to the age of 18 years, \( P_{(st)} \) has been shown to increase linearly (104) although there is a tendency for this to be curvilinear (156). The increase in elastic recoil reflects the change in the amount and distribution of the elastic tissue within the lung (119). During alveolar multiplication there is an increase in the total amount of connective tissue in the lung, the distribution of which alters when the alveoli rapidly expand. The closing volume \( (CV) \) has been shown to decrease with increasing age in children and the \( P_{(st)} \) correlates inversely with \( CV \) (104). Although there is an increase in the elastic recoil during growth, there is little change in the lung compliance when expressed in terms of lung size (specific compliance) (24). Similarly, elastic recoil is related to stature, so that \( P_{(st)} \) increases with height but when expressed in terms of
lung volume \([P_{st}\)/TLC] the retraction co-efficient\), it is independent of stature (3).

Elastic recoil influences the subdivisions of lung volume as it is an integral part of the balance of forces operating within the thorax. The functional residual capacity (FRC) and residual volume (RV) are particularly affected by a change in the elastic recoil. In adults, the ratios RV/TLC and FRC/TLC both increase with age as the lung loses its elasticity, with the chest wall becoming increasingly rigid due to the increase in the thoracic elasticity (157). In children, however, the elastic recoil of the lung increases with growth as the lung develops and expands to increase its volume. Consequently, the ratios RV/TLC and FRC/TLC remain constant throughout childhood (37). The relative change in the subdivisions of lung volume is illustrated in Fig 2.2.

2.6 **Puberty**

The description of lung growth and development would not be complete without mentioning the changes that occur at puberty. Puberty is defined as the transitional period between the juvenile and adult during which the appearance and maturation of secondary sex characteristics occur, the adolescent growth spurt takes place, fertility is attained and profound psychological changes transpire (72). Of these, it is the adolescent growth spurt that accounts for the changes in lung development during this period. Up to the time of puberty there is little difference between the sexes, except that boys generally have larger lungs by an average of 8% and display larger lung function indices as a result (37). During adolescence the difference between the sexes becomes more marked and remains so throughout life. (A good reason for rejecting the approach of putting sexes together in one prediction equation). The onset of puberty is more closely linked to height than chronological age. At a height of 152cms in both sexes the vital capacity (VC) and expiratory flow rates (PEF, \(V_{50}\), \(V_{75}\)) start to increase rapidly (48). The difference in size between men and women is mainly due to the difference in the timing and intensity of the adolescent growth spurt (147). The sexual differences between the onset of
puberty is about 2 years, the age of the peak development is 14.1 ± 1.3 years in boys and 12.1 ± 1.4 years in girls (148). Apart from this later onset, boys also have a far more intensive growth spurt showing greater peak velocity changes than girls (height peak velocity - boys 10.3 ± 0.22 cm.yr⁻¹, girls 9.0 ± 0.16 cm.yr⁻¹; weight peak velocity - boys 9.8 ± 0.30 kg.yr⁻¹, girls 8.8 ± 0.25 kg.yr⁻¹ (149, 151). Boys, therefore, have longer to develop before puberty and then have a more intensive adolescent growth spurt. The usual pattern of growth exhibited by most functional measurements is that boys begin larger and are then overtaken by girls who enter puberty earlier. Later, boys again overtake as they have a late, more intensive growth period. The sexual differences then remain throughout adulthood. The lung dimensions, however, as reflected by lung width and lung length are unusual in that girls never exceed boys in their values. Only head measurements and foot length show a similar pattern (82).

It is important to realise that lung development during the adolescent growth spurt is linked to the level of physical activity during this time. Training improves the size and function of the lung. Also during the adolescent growth spurt the change in height is mainly due to growth of the trunk rather than leg growth. Consequently, sitting height can be used as an acceptable alternative to height as a reference value during puberty (133).

2.7 Summary

The anatomical and functional development of the lung during the period of growth have been summarised, with particular reference to the elastic properties of the lung. Measurements of lung function indices have been shown to reflect the underlying pattern of growth and mirror the trends in physiological development. In this way lung function indices can be used to determine changes occurring over time.
CHAPTER 3

BASIS FOR THE RESEARCH PROGRAMME
3.1 Introduction

There have been many studies to monitor growth from childhood to adulthood, the most comprehensive of which have been longitudinal surveys of the entire period of growth (150, 151). Growth curves have been fitted to the data (9, 150).

Lung function measurements have been reported in the literature for almost every year of man's life span, from neonate to geriatric despite the difficulties in obtaining these measurements in the very young and very old. The purpose of measuring lung function in these surveys has been to produce valid and useful prediction equations enabling an individual's lung function at any time to be assessed from other variables associated indirectly with the lung (77, 132). Age and height are the most reliable predictors of lung function in the adult; chronological age does not contribute as much to the description of lung growth in childhood (39, 132). Lung development proceeds as a function of somatic growth rather than as a simple function of age. Most lung function studies were not designed to specifically investigate lung growth, and it is not surprising, therefore, that descriptions of lung growth are not forthcoming from their data. Moreover, lung function data in the literature are derived predominately from cross-sectional studies (27, 49, 86, 90, 130, 145, 166). These are easier to conduct and less costly than longitudinal surveys (70, 125, 134), but may not reveal important trends underlying growth as the data are collected over shorter period of time from unassociated individuals (65, 90).

The purpose of the research programme reported in this thesis was to describe and explain the development of the lung in adolescent men between the ages of 17-19 years. The term adolescent is used in order to avoid confusion with studies using 'young adults' - these usually refer to individuals greater than 20 years of age.
The previous chapters have reviewed the literature and described the major concepts in the field of lung growth. In undertaking this research programme the following hypotheses were addressed:

1) can the increase in lung size be accounted for adequately by the increase in stature?

The measurement of height is the most commonly obtained anthropometric variable. It is used to predict lung function and is considered more useful than age as an indicator of lung size. In prediction equations lung size is related to height cubed in children and height squared in adults (120). However, as already discussed, the lung is unlikely to develop according to precise symmetry. The lung may develop between the ages 17-19 years so that the increase in lung size is not adequately accounted for by the increase in stature.

ii) do different subdivisions of the lung volume grow at the same rates?

The volume of air contained within the developing airways and alveoli is reflected by lung size. It is important to assess whether increases in lung size are proportionally distributed between the volume subdivisions of TLC. Different rates of increase in volume may reflect disassociation between growth patterns in the lung.

iii) can the increase in lung size be attributed to an increase in the thoracic dimensions?

If height does not solely predict the increase in lung size between 17-19 years, then the inclusion of thoracic dimensions may improve the prediction equations. Chest width is thought to be particularly associated with lung growth and certainly the thoracic dimensions increase with somatic growth (29). This has important implications as chest width and chest depth are not currently considered as routine survey measurements.
iv) is the increase in chest volume due to lowering of the diaphragm?

Any change in resting lung volume may be associated with a change in the volume of the thorax. Changes in the volume of the thorax may occur due to growth of the chest wall or a change in the position of the diaphragm. This may be assessed by equating the percentage increase in chest volume with the associated percentage increase in the resting lung volume. If they are similar the increase in chest volume is not due to the lowering of the diaphragm.

v) is there a change in the lung elastic recoil associated with lung growth?

The connective tissue network in the lung has been associated with alveoli development. It is integrally involved in the structure of the alveolar wall and parenchymal tissue (section 1.7). Lung growth may be associated with a change in the distribution and abundance of the connective tissue fibres. This would alter the lung elasticity as measured by the lung elastic recoil.

vi) does the lung expand or grow within the larger thoracic cavity during development?

There is an increase in chest volume during the period of growth. If this occurs during the ages of 17-19 years the lung may expand to fill the enlarged thoracic cavity or grow by the hypertrophic and hyperplastic development of the alveoli discussed previously (48). This may be assessed by the change in the subdivisions of TLC when expressed as a percentage of total lung capacity.

vii) does the lung increase in size as a result of changes in the elastic properties of the respiratory system?

The change in the elastic properties of the respiratory system (which includes the chest wall elasticity) may result in the increase in lung size associated with lung growth. Total lung capacity and proportions of its subdivisions depend on the mechanical balance between the elastic forces of the lung and
thorax (157) and the increase in thoracic dimensions may be due to an increase in the outward recoil of the chest wall. The importance of the mechanical properties of the rib cage during growth has been discussed in Chapter 2 (section 2.3).

viii) is there an association between the size of the trachea and the size of the lung?

The conducting airways contribute to the increase in lung volume associated with growth. If this growth is dysanaptic (different branches of the airway grow at different rates) then there will be no association between large airway size and lung volume (68, 88). This has been demonstrated by others using tracheal dimensions and cross-sectional area (35, 51, 84, 90).

ix) do differences in physical activity and muscular strength contribute to the differences in lung growth between individuals?

The respiratory muscles increase in muscular strength with age (24). This is associated with the increase in lung size during growth and it has been reported that increasing muscle strength by training or exercise may improve the size of the lung (117). This is of importance when interpreting the cause of differences in lung growth between individuals.

3.2 The Longitudinal Study

The research was designed as a longitudinal survey although drawbacks have been cited in their use (5, 71). To outline the growth of the lung in the 17-19 year old age group longitudinal data were available from apprentices at British Shipbuilders, Wallsend Shipyard. In such a working population, taking measurements of lung function annually in each individual was more practical than at six-monthly intervals although the latter would have been preferable (136).

The 17-19 year old age group was chosen as this is an interim period of development. It occurs after the 'adolescent growth spurt', which is characterised by peak velocity increments in growth variables, and before the functions of the lung decline
with age. In order to produce prediction equations, the age groups studied in other lung function surveys have related to either paediatric populations or adult populations; in the former, lung function indices increase with growth (67, 76) and decrease with advancing age in the latter (40, 130, 166). The paediatric populations do not usually extend at their upper age range to include 17 year olds and the adult populations usually begin at ages greater than 20 years. In the relatively few studies where 17-19 year olds have been included as the extreme age group the prediction equations produced have been of limited value in describing their lung function (47, 98, 137, 141, 158, 161). There are only a few studies which attempt to bridge the gap between paediatric and adult lung function (27, 30, 106). It was thought that the decline in lung function due to aging began in the late teens - early twenties and this would confound the interpretation of prediction equations during this period (48, 140). It now appears that the lung function indices begin declining at a much later age, possibly as late as the mid-thirties (6, 25, 97), but earlier decline may occur in smokers (152).

To determine growth of the lung during this period, the measurements obtained from the British Shipbuilders apprentices were chosen carefully to reflect lung maturation. The volume of air contained within the lung is indicative of the size of the lung. To demonstrate the increase in lung size due to growth, the static lung volumes were obtained to give total lung capacity (TLC) and its subdivisions. To describe somatic growth, as an indicator of lung growth, it is useful and necessary to take measurements of anthropometric variables in lung function surveys. Commonly, height is monitored as an effective predictor of lung function but few studies have included measurements of thoracic dimensions (134). The longitudinal survey presented in this thesis has lung growth reflected by lung volume measurements and somatic growth by anthropometric measurements which include chest width, chest depth and sternal length. In this way a detailed description of growth of the lung and thorax was obtained concurrently. It was envisaged that an increase in lung size may be influenced by factors other than simply lung growth.
It was unlikely that disease would play a major role in the development of a young healthy population of 17-19 year olds, but smoking, especially in this age group, may have been very important. Physical activity, training and an increase in muscular strength may also be factors which affect lung development (25, 117, 136). For this reason measurements of respiratory muscle strength (maximal respiratory pressures) were included in the survey for the second year interval (18-19 years). A respiratory questionnaire (MRC, 1976) was also completed to provide clinical and smoking histories, although no subject was excluded due to smoking criteria.

3.3 The Cross-sectional Study

The longitudinal survey provided details of lung development during the ages 17-19 years in a growing population. It has been demonstrated that as adolescents grow older they have a greater lung volume using equations developed for children based on their height (38, 47). There is also evidence that the vital capacity continues to increase even when height measurements have stopped improving (57, 98). This suggests that there is some degree of lung maturation not explained by growth. To investigate this imbalance between lung size and somatic growth a cross-sectional survey was designed and undertaken after the longitudinal survey had been completed. The purpose of this cross-sectional study was to interpret the phenomenon of different lung sizes in individuals with similar heights (44).

It is possible that individual differences in lung sizes at age 19 years may be due, in part, to changes in the elastic properties of the respiratory system. This has been cited in the literature as a worthwhile field of study as no data has been published on the subject (136). To investigate this aspect of lung maturation the measurement of lung distensibility (lung compliance) had to be obtained. As this could not be introduced retrospectively into the longitudinal survey, a cross-sectional population was selected from the men in the longitudinal survey at 19 years. They were selected on the basis of their lung size being greater or less than that predicted based on their individual height. This yielded two sub-groups, both with
similar height, age and most other variables except lung size. On these adolescents measurements of lung compliance and elastic recoil were obtained to add to the data already available from the longitudinal survey. In addition there was an opportunity to obtain measurements of upper airway size in these men. Lateral and postero-anterior chest X-rays were obtained from which tracheal area and diameters were measured. There has been much interest in the literature in recent years with respect to tracheal diameters (23, 89, 100, 160). The change in tracheal dimensions with age (60) and height (69), and the contribution attributed to the large airways in the measurements of air flow have led to increased reporting of tracheal data (51, 57, 116). By relating tracheal diameters to lung size most authors agree that the lung grows dysanaptically. In this thesis the tracheal dimensions are presented to reflect the influence of the pleural pressure within the thoracic cavity. The trachea is an extra-pulmonary structure so that its dimensions are influenced by the intrathoracic pressure. This is determined by the pleural pressure and can be measured at TLC.

In summary, the purpose of the cross-sectional study was to investigate whether lung development in individuals of the same height was due to changes in the elastic forces of the respiratory system. This followed a description of lung growth in a longitudinal survey of 17-19 year old male adolescents. The findings of both studies are presented in this thesis.
CHAPTER 4

METHODS AND MATERIALS
4.1 Subjects

4.1.1 Longitudinal Study

The subjects in this study were 269 newly recruited male apprentices employed by British Shipbuilders. The medical examination required for entry by British Shipbuilders was rudimentary. All the men were residents in the Tyneside area and intended to train for skilled jobs in heavy industry. (As the results will strictly apply to this population only, a detailed demographic description of the men is given in the results). The management agreed to allow the apprentices to take part in an epidemiological survey involving longitudinal measurements of lung function. It was agreed that the measurements be taken on an annual basis. This study began when the men entered their apprenticeship at 16 years of age and each subject was allowed time off work for the measurements to be taken. In the first year the men were seen in a training centre where they were collectively employed in the same area. The lung function equipment for the study was housed in two rooms in the training centre. The first series of measurements were taken over a three month period and the number of men seen represents the entire intake of apprentices for that year. In the remaining years of their apprenticeship the men were trained in four shipyards on the River Tyne. It became more difficult to locate and study them as they were periodically transferred for work between the four shipyards. A mobile laboratory was used to house the lung function equipment for the study and was towed to each shipyard in turn. Repeat measurements were obtained on as many of the men as possible. The second series of measurements was obtained over a nine month period and the third series of measurements over a period of seven months.
4.1.2 Cross-Sectional Study

The men for the cross-sectional survey were a sub-population of the men participating in the longitudinal survey. These men were chosen because their lung volume, as determined by total lung capacity (TLC), was larger or smaller than predicted based on their height at the time of the study. These men represented the extreme samples from the normal distribution of observed minus predicted lung volumes.

There were 198 men in the longitudinal survey population with data for the third year for study. The linear regression for total lung capacity (TLC) based on stature using data from the third year of study was:

\[
\text{TLC(l)} = 7.93 \text{ stature(m)} - 7.49 \pm 0.62(1) \quad r = 0.667
\]

This represented the prediction equation for TLC for the total population and the standard deviation of the equation is 0.62 litre.

It was then calculated that a standardised normal deviate of 0.843 SD would select 20% of the longitudinal survey population with a TLC greater than predicted at the extreme of the normal distribution and 20% of the population with a TLC less than predicted at the other extreme of the distribution. Thus men were selected whose observed TLC was greater or less than the predicted TLC by 0.523 litre (0.843 x 0.62)

In total, approximately 40% of the longitudinal survey population of 198 men were selected for the cross-sectional study. Each subject was approached and asked to volunteer for the study. They were asked to attend one session in the laboratory at Newcastle University and one session at Wallsend Chest Clinic to have chest X-rays taken. Both these occasions were outside normal working hours so that permission from the shipyard management was unnecessary although ethical committee approval was obtained.
4.2 Lung Volumes

4.2.1 Longitudinal Study

The subdivisions of total lung capacity (see Fig 2.1) were measured according to standard procedures (37). A detailed description of the methods may be found in Appendix 1.

The lung volumes were determined using a Resparameter Mk 4 (P.K. Morgan Limited) which was used in closed-circuit mode. The apparatus was checked to be airtight on a twice-daily basis. Calculation of the 'dead space' of the apparatus was obtained daily and whenever the volume of the internal soda-lime canister was altered. Details of both these procedures may be found in Appendix 2.

Direct measurements of lung volumes were taken from the conventional spirogram obtained from the Resparameter (Fig 4.1). These were:

- Expiratory Reserve Volume (ERV)
- Inspiratory Capacity (IC)
- Expiratory Vital Capacity (EVC)
- Inspiratory Vital Capacity (IVC)

To obtain the lung volumes that could not be directly measured from the Resparameter trace, the helium dilution method was used to give:

- Functional Residual Capacity (FRC)

The following lung volumes were then calculated according to:

- Residual Volume (RV) = FRC - ERV
- Total Lung Capacity (TLC) = EVC + RV
- Residual Volume as a percentage of TLC (RV%) = RV x 100/TLC
4.2.2 Cross-Sectional Study

The Resparameter kymograph trace was recorded at the laboratory session in the cross-sectional study (FRC and RV were not obtained directly as the helium dilution technique was not applied) (Fig 4.1).

4.3 Maximal Respiratory Pressures

The maximal pressures recorded at the mouth at full expiration and full inspiration were measured using standard procedures (10).

The maximal respiratory pressures were recorded using a closed tube system (length 15cm, diameter 3cm) attached to a rigid mouthpiece.

The subject was seated and asked to hold the mouthpiece near to the mouth ready for the test. Great care was taken to demonstrate how to place the rigid mouthpiece in the mouth to avoid leaking air from around the lips. It was also emphasised that the subject should not inspire or expire after being told, by the observer, to put the mouthpiece in position. The mouth pressures were recorded on a differential pressure transducer (Mercury M8, range 0 - 29.4 kPa) and plotted on an x-y/t recorder at chart speed 2.5 s.cm\(^{-1}\). The pen of the plotter was set down for baseline recording prior to the test manoeuvres. The pressure transducer was calibrated daily with a mercury manometer.

1) Maximal Expiratory Pressure (MEP)

The subject was asked to inhale to the greatest possible extent and after that to place the mouthpiece in his mouth. He was told to try and breathe out as hard as possible, for as long as possible, against the resistance. These instructions were given before the test began, and again during the test when the subject was encouraged to perform maximally. Two hypodermic needles were introduced, via a rubber bung, into the mouthpiece system. This was to allow a very small volume of air to leak from the tubing so that the cheek muscles were not extended to influence the
FIG. 4.1  EXAMPLE OF KYMOGRAPH TRACE OBTAINED FROM LUNG VOLUME PROCEDURE

He₁  initial helium reading
He₂  final helium reading
V₁  initial volume reading
V₂  final volume reading

\[
\text{FRC}(1)(\text{BTPS}) = \frac{\text{He}_{1}(V_{1} + DS) - (V_{2} + DS)}{\text{He}_{2}} \times \text{correction factor}
\]

where:- DS is the dead space of the resparameter in litres

'flushing out'
pressure measurement. Maximal mouth pressures were acceptable if they were sustained for one second and the greatest value from three satisfactory test manoeuvres was taken.

2) **Maximal Inspiratory Pressure (MIP)**

The rubber bung with the hypodermic needles was removed from the mouthpiece system as there was no need to allow for pressure exerted by the cheek muscles in this manoeuvre. It was replaced with an intact rigid rubber bung. The subject was asked to breathe normally and, when indicated by the observer, stop breathing and place the mouthpiece in the mouth. He was then asked to 'suck in' as hard as possible from the enclosed tube. The observer initiated this procedure when the subject was at functional residual capacity (FRC) as judged by movement of his chest wall during quiet breathing. By close observation it could also be ascertained whether breathing occurred after the instruction to place the mouthpiece in the mouth. Most subjects found this manoeuvre more difficult than the maximal expiratory pressure test but all subjects gave three satisfactory recordings. Care was taken at the time of measurement to mark traces as unsuitable when evidence of the 'straw-effect' occurred. This could be seen as over-suction at the beginning of the trace due to pharyngeal muscle action (Fig 4.2). The highest pressure recorded over one second from three satisfactory manoeuvres was taken.

4.4 **Additional Measurements in Longitudinal Study**

4.4.1 **Anthropometry**

Anthropometric measurements were obtained using standard procedures (162). These are summarised below.

The stature, floor to sternal notch and sitting height measurements were recorded using a Harpenden Stadiometer (Holtain Limited) which was calibrated daily using a standard length rod (600mm). The maximum of two readings was taken.
FIG. 4.2  EXAMPLE OF RESPIRATORY PRESSURE TRACE
(Inspiratory Effort)

1 sec
Pressure (kPa)
Baseline

Pharyngeal muscle action to increase pressure momentarily

Trace Disregarded
Baseline
The other variables were recorded using a portable, hand-held Harpenden Anthropometer (Holtain Limited) with interchangeable straight or recurved blades of adjustable length. The counter on the anthropometer was inspected daily and care was taken to hold the body of this instrument parallel to the body-axis in the plane of measurement. The mean of two consecutive readings, that agreed to within 5mm, was taken.

The skinfold thicknesses were taken on the left hand side of the body. They were measured using Holtain calipers and the spring tension was adjusted to exert a pressure equivalent to a suspended 60g weight. Using the left thumb and forefinger the observer picked up the skinfold 0.5cm above the point of measurement. The caliper jaws were applied and, after 2 seconds, the reading was taken. The delay provided a standard time for the displacement of tissue fluid. The mean of two consecutive readings, which agreed to within 0.5mm, was recorded.

All the measurements were recorded in millimetres and corrected to centimetres and metres where appropriate. They are listed in Table 4.1.

Each subject removed his boots and stripped to the waist. Standing with his feet approximately 25cm apart the body was strategically marked with a demographic pencil (Appendix 3).

1. **Body Mass (BMASS; kg)**

   The subject was weighed to record body weight. This was achieved on an Avery beam balance correctly calibrated weekly with standard 25kg weights and the 'zero' checked on a daily basis.

2. **Stature (STAT; m)**

   The subject stood with his feet together and his heels against a wooden block at the base of the Harpenden stadiometer. The posture was manipulated so that the spine
TABLE 4.1

Anthropometric Measurements and their abbreviations

<table>
<thead>
<tr>
<th>MEASUREMENTS</th>
<th>Abbreviation</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Mass (weight)</td>
<td>BMASS</td>
<td>kg</td>
</tr>
<tr>
<td>BODY LENGTHS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standing height (stature)</td>
<td>STAT</td>
<td>m</td>
</tr>
<tr>
<td>Floor to sternal notch</td>
<td>FTOS</td>
<td>m</td>
</tr>
<tr>
<td>Sitting height</td>
<td>SITHT</td>
<td>m</td>
</tr>
<tr>
<td>THORACIC DIMENSIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left costal margin length</td>
<td>LCML</td>
<td>cm</td>
</tr>
<tr>
<td>Right costal margin length</td>
<td>RCML</td>
<td>cm</td>
</tr>
<tr>
<td>Sternum length</td>
<td>STERNL</td>
<td>cm</td>
</tr>
<tr>
<td>Chest width</td>
<td>CHW</td>
<td>cm</td>
</tr>
<tr>
<td>Chest depth</td>
<td>CHD</td>
<td>cm</td>
</tr>
<tr>
<td>BODY WIDTHS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder width</td>
<td>SHW</td>
<td>cm</td>
</tr>
<tr>
<td>Hip width</td>
<td>HIPW</td>
<td>cm</td>
</tr>
<tr>
<td>SKINFOLD THICKNESS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biceps skinfold</td>
<td>BI</td>
<td>mm</td>
</tr>
<tr>
<td>Triceps skinfold</td>
<td>TRI</td>
<td>mm</td>
</tr>
<tr>
<td>Subscapular skinfold</td>
<td>SUB</td>
<td>mm</td>
</tr>
<tr>
<td>Suprailliac skinfold</td>
<td>SUP</td>
<td>mm</td>
</tr>
<tr>
<td>DERIVED MEASUREMENTS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage body fat</td>
<td>FAT %</td>
<td>%</td>
</tr>
<tr>
<td>Fat free mass</td>
<td>FFM</td>
<td>kg</td>
</tr>
</tbody>
</table>
was as straight as possible and the heels, buttocks and shoulders were in contact with the backboard of the stadiometer. The subject was asked to adopt a natural position with the shoulders relaxed to minimise spinal curvature. The arms and hands were relaxed so that the palms of the hands were not held in the anatomical position but faced medially. The counter-weighted board of the stadiometer was brought down on the subject's head which was positioned in the Frankfurt plane. (The lower border of the orbit being horizontal in line with the upper margin of the external auditory meatus). Gentle upward traction was applied to the mastoid process, by the observer, to extend the subject to the greatest height attainable. Care was taken to ensure that the subject's heels did not leave the floor. The height was then read directly from the counter on the stadiometer. It was necessary for the observer to kneel on a stool to ensure that the counter could be read at eye level and the posture manipulated correctly.

3. **Floor to Sternal Notch (FTOS; m)**

The subject was asked to stand so that one corner of the counter-weighted board of the Harpenden stadiometer rested on the marked level of the suprasternal notch (the superior aspect of the sternum). In order to achieve this posture the subject had to stand at a 45° angle to the stadiometer and care was taken to ensure that the long axis of the body remained parallel to the apparatus. The posture adopted was the same as for the measurement of stature, feet together and shoulders relaxed.

4. **Sitting Height (SITHT; m)**

The subject was seated on a flat topped stool of known height (stool height = 608 cm). This stool was placed at the base of the Harpenden stadiometer and the seated subject asked to relax the buttocks and thighs to let the legs hang freely. The back was as straight as possible with the shoulders relaxed. The backboard of the stadiometer was in contact with the sacral and intrascapular regions. The
observer again positioned the subject’s head in the Frankfurt plane and applied gentle traction to the mastoid process to achieve the greatest height possible. The stool height was regularly checked after the Harpenden stadiometer had been calibrated with the standard length rod.

5. **Right/Left Costal Margin Length (RCML/LCML; cm)**

The observer stood in front of the subject holding the anthropometer in a vertical position. Straight blades were fitted and the tip of the upper blade was placed above the mid-clavicular mark (Appendix 3). The lower blade was placed on the mark at the lower edge of the costal margin. The procedure was performed on the right and left hand side of the body. The measurements were rechecked when there was a difference of >5mm between right and left sides.

6. **Sternum Length (STERNL; cm)**

The anthropometer, fitted with straight blades, was held as described in the previous section. The upper blade was pressed down on the superior aspect of the sternum. The tip of the lower blade was placed on the mark coinciding with the base of the xiphoid process.

7. **Chest Width (CHW; cm)**

The observer stood in front of the subject holding the anthropometer horizontally. Recurved blades were fitted and the subject held his arms away from his body for this measurement. The point of each blade was applied at the level of the 5th rib, in line with the nipples, in the coronal plane. The blade points were moved superio-inferiorly over the ribs and the measurement was recorded at its highest value; this relates to the greatest transverse chest diameter at this particular level.

8. **Chest Depth (CHD; cm)**

The subject stood with his right hand side facing the observer. The anthropometer, fitted with recurved blades, was held horizontally. The blades were applied to the
anterior surface of the sternum and the posterior aspect of
the spinous process of the corresponding thoracic vertebra
in the median sagittal plane.

9. **Shoulder Width (SHW; cm)**

The subject stood with his back to the observer, who knelt
on a stool for eye level reading of the anthropometer
counter. The most lateral edges of the acromium processes
were located as a ridge of the scapular just above the
shoulder joint. The blades of the anthropometer were moved
over this ridge so that the largest excursion of the blades
gave the biacromial diameter.

10. **Hip Width (HIPW; cm)**

With the subject holding his arms horizontally and with his
back to the observer, the anthropometer blades were applied
to the iliac crests and moved superio-inferiorly to achieve
a maximal excursion. Strong pressure was then applied in
order to displace the soft tissue. This gave the
biiliocristal diameter.

11. **Biceps Skinfold (BI; mm)**

The subject stood with the arms in the anatomical position
(the palms of the hands facing forward). The forearm was in
full supination. The skinfold was taken at the level of the
horizontal mark on the left upper arm over the biceps
brachii muscle.

12. **Triceps Skinfold (TRI; mm)**

The subject stood so that the palms of the hands faced
medially. The forearm was in between pronation and
supination. The skinfold was taken at the level of the
horizontal mark on the left arm in line with the olecranon
process over the triceps brachii muscle.
13. **Subscapular Skinfold (SUB; mm)**

The subject stood relaxed and the skinfold was taken 2cm inferiorly and 2cm laterally from the inferior angle of the scapular. It was taken obliquely to coincide with the fibre course of the underlying latissimus dorsi muscle.

14. **Suprailiac Skinfold (SUB; mm)**

The subject stood with the trousers lowered. The skinfold was taken 2cm superiorly and 2cm medially from the anterior, superior iliac spine. It was taken obliquely to coincide with the fibre course of the external oblique muscle.

15. **Derived Anthropometric Indices**

The sum of the four skinfold measurements was used to calculate body density and hence **Percentage Fat (FAT%)** and **Fat Free Mass (FFM; kg)** from the equations derived from the data of Durnin and Wormersley 1974 (54).

\[
\text{Body Density} = 1.18 - 0.000549(\text{Age}) - 0.06484 \log (\text{sum of skinfolds})
\]

\[
\text{Fat \%} = \left| \frac{4.95 - 4.5}{\text{Body Density}} \right| \times 100
\]

\[
\text{FFM} = \text{B MASS} - \text{FAT}%
\]

4.4.2 **MRC Questionnaire on Respiratory Symptoms**

The Medical Research Council questionnaire on respiratory symptoms (UK 1976) was used to provide information on symptoms, respiratory illness and smoking habits. Additional questions regarding sporting activity were also asked to ascertain the level of physical activity undertaken by the subjects. These showed whether the men were in training for competitive activities.
4.5 Additional Measurements In Cross-sectional Study

In the laboratory session the measurements of stature (STAT; m) and body weight (BMASS; kg) were obtained as described previously.

4.5.1 Pressure-Volume Curve Measurements

Measurements of the elastic properties of the lung were obtained using standard procedures (61). A detailed description of the method may be found in Appendix 4. The apparatus is illustrated in Fig 4.3.

Static pulmonary compliance and elastic recoil of the lung were measured using the interrupter method with a shutter duration of one second. Volume was recorded using a dry bellows spirometer (McDermott) calibrated using a 3-litre syringe. Transpulmonary pressure was recorded using a differential pressure transducer (Mercury MU/21078, range 0-2.9 kPa). This was calibrated using a water manometer on the day of testing.

An oesophageal balloon (length : 10cm; perimeter: 2.5cm; balloon volume : 0.4ml) was introduced into the subject's lower-third oesophageous via the nostril. The depth was adjusted so that the most negative pressure was recorded during sniffing and the cardiac artefacts were negligible (usually 38-42cm from the nares) (61). The subject wore a noseclip to secure the placing of the balloon throughout the test.

1) Expiratory Compliance ($C_{EXP}; 1\text{kPa}^{-1}$)

After three vital capacity manoeuvres to ensure a constant volume history the subject expired slowly from TLC into a bellows spirometer. The expiration was interrupted at one second intervals by a shutter mechanism within the system (Fig 4.3). The shutter remained closed for a period of one second on each occasion. At least two satisfactory expiratory pressure-volume curves were obtained from which the expiratory compliance ($C_{EXP}$) was measured as the
FIG. 4.3  DIAGRAM OF THE APPARATUS TO MEASURE LUNG ELASTICITY

Lung Compliance = \Delta V / \Delta P = 1 \text{ kPa}^{-1}

where

- \Delta V is the change in lung volume
- \Delta P is the change in transpulmonary pressure
gradient of the curve over its linear portion (Fig 4.3). The mean value of expiratory compliance ($C_{\text{EXP}}$) was calculated.

2) **Inspiratory Compliance ($C_{\text{INS}}; 1.\text{kPa}^{-1}$)**

The subject inspired from residual volume (RV) to TLC very slowly with the shutter system in operation so that at least five pressure-volume points were recorded during the manoeuvre. At TLC the subject held the position with the glottis open for 2-3 seconds and then came off the mouthpiece. At least two satisfactory inspiratory pressure-volume curves were recorded and the inspiratory compliance ($C_{\text{INS}}$) measured as the gradient of the curve over its linear portion (11). The mean of the values obtained was calculated.

3) **Maximal Recoil Pressure (RP; kPa)**

At full inspiration (TLC) on the inspiratory pressure-volume curves the maximal pressure recorded when the shutter was closed was measured. This gave the maximal recoil pressure denoted by RP. The maximal value was taken from the satisfactory inspiratory pressure-volume curves.

4) **Recoil Pressure at TLC-20%VC ($P_{\text{STAT}}$; kPa)**

The expiratory pressure-volume curves were used to calculate the pressure obtained when the subject had expired 20% of the vital capacity from TLC. If no shutter point had occurred at this volume, the exact point on the curve was accepted as the pressure measurement. The mean value from the satisfactory expiratory pressure-volume curves was calculated as $P_{\text{STAT}}$.

5) **Recoil Pressure at FRC ($E_{\text{FRC}}, I_{\text{FRC}}$, kPa)**

The recoil pressure at FRC was determined from the pressure-volume curves. The mean from at least two satisfactory expiratory curves gave $E_{\text{FRC}}$ and the mean from at least two satisfactory inspiratory curves gave $I_{\text{FRC}}$. 

- 53 -
6) Calculation of Standardised Lung Compliance

Lung compliance is dependent on lung size. To allow for the differences in lung volumes between the subjects the lung compliance was standardised using a derived measurement of TLC.

The total lung capacity was not measured at the laboratory session in the cross-sectional survey. Each man had previously had three annual measurements of TLC taken in the longitudinal survey and a fourth obtained after the cross-sectional survey was completed. This fourth measurement was a continuation of the longitudinal epidemiological study. An estimate of the TLC from each subject at the time of the laboratory session in the cross-sectional survey was obtained using regression analysis. For each man the TLC against age regression equation was plotted using the method of least squares to fit the regression line. Knowing the age at which the subject attended the laboratory his TLC at this point could be calculated from his individual regression equation. In this way specific compliance \( C_{EXPTLC}; C_{INSTLC}; \frac{1}{kPa}\cdot\frac{l}{TLC} \) was calculated.

To provide a more accurate method of standardising the lung compliance for difference in lung volumes, the pressure-volume curves were replotted. Each point on each curve was redefined as pressure (kPa) against %TLC according to the individual's TLC on the day of testing. The curves were then redrawn and a line fitted to the linear portion using the method of least squares. Lung compliance, expiratory and inspiratory, was then calculated according to the procedures already described \( C_{ETLC}; C_{ITLC}; \frac{\%TLC}{kPa} \). The results were expressed as a %TLC volume change rather than a litre volume change for a given change in pressure (61).

4.5.2 Chest X-ray Measurements

The subject stripped to the waist and had lateral and posterio-anterior chest radiographs taken in the standard
postures adopted for this procedure. The focus to film distance was 1.83 metres and the radiographic film was over-penetrated (75kv, 6 m.a.s., Kodak 091 film) for more accurate determination of the tracheal borders. Metal markers of known diameter (10 pence coins) were placed on the chest to determine the magnification factors (Appendix 5).

1) **Tracheal Diameter from Posterior-Anterior X-rays (PTD; cm)**

The lateral tracheal diameter (PTD) was obtained from the posterior-anterior chest X-rays. This was taken when the subject was at full inspiration (TLC). One coin was placed anteriorly on the chest on the left hand side of the body. Another was placed posteriorly on the back of the body on the right hand side. Both were placed in the same plane of measurement. The tracheal diameter was determined by two independent observers from the X-ray. A 4 cm segment of trachea was traced, the lower border of which was taken as 2.5 cm above the carina. Every 0.5 cm a diameter was measured so that the PTD was taken as the mean of 9 values over the length of the segment (Fig 4.4). This was according to standard procedures described elsewhere (60). The actual tracheal diameter (PTD) was the measured value from the X-ray multiplied by the magnification factor (Appendix 5) (91). The trachea was assumed to be positioned as the bisector of the line between the two metal markers for the calculation of focus to object distance (F.O.D.).

2) **Tracheal Diameter from Lateral X-rays (LTD; cm)**

The posterior-anterior tracheal diameter (LTD) was obtained from lateral chest X-rays taken at TLC. The coin marker was placed over the sternum in the 'nipple-line' to determine the magnification (Appendix 5). The trachea was assumed to be positioned in this plane for the calculation of the magnification factor using focus to object distance (F.O.D.). The tracheal diameter was determined by two independent observers from the chest X-rays. A 4 cm tracheal segment was traced, the lower border of which was taken as
FIG. 4.4  EXAMPLE OF TRACHEAL TRACING FROM CHEST X-RAYS

Posterior - Anterior X-Ray

Lateral X-Ray

PTD = 1.7 cm x magnification factor

LTD = 2.0 cm x magnification factor
2.5 cm above the left pulmonary artery. The same method of measurement was adopted as described for the lateral tracheal diameter and illustrated in Fig. 4.4.

The tracheal diameters (PTD, LTD) were taken as the mean value obtained by the two observers.

3) Tracheal Cross-Sectional Area (XTRAC; cm$^2$)

The cross-sectional area of the tracheal is calculated based on the trachea being an ellipse:

Area of Ellipse = $\pi a b$.

\[
XTRAC =\frac{\pi}{2} \cdot \frac{LTD}{2} \cdot \frac{PTD}{2} \quad (cm^2)
\]

4.6 Reproducibility of the Methods

The methods described for the measurements of lung compliance, elastic recoil and anthropometric thoracic dimensions were repeated in the same individuals on two separate occasions to assess the reproducibility of the procedures. Details of the assessments and the results are given in Appendix 6.

4.7 Statistical Analysis

The results were analysed using standard parametric and non-parametric statistical tests available in the Statistical Package for the Social Sciences (SPSS)(112, 115). This statistical package was installed on a Hewlett Packard Vectra drive computer so that the data were stored on 4" floppy disks. (The data had been stored previously on magnetic disks in the mainframe IBM computer at Newcastle University).

The data were analysed by descriptive statistics and comparisons made using Student's t-test. The null hypothesis was rejected if the significance level of 5% was achieved ($p < 0.05$). Where multiple regression analysis was performed the variables were
entered into the equation by forward stepwise regression. Correlations and associations between variables were determined by the correlation coefficients generated by a Pearson correlation matrix. The percentage change for measurements was calculated as: $\frac{\Delta x}{x} = \frac{\Delta x}{\bar{x}}$ (115).

The data were set and stored after analysis into an SPSS systems file for future access.
5.1 Reproducibility Of The Methods

The measurements of lung compliance, elastic recoil and thoracic dimensions were repeated in a group of subjects to assess the reproducibility of the methods. The procedure and results are given in Appendix 6.

There were no significant differences between the pressure-volume curve measurements taken on the two separate occasions (p > 0.05) and the correlation coefficients indicated a close relationship between them (r > 0.7). However, the recoil pressure at TLC - 20%VC ($P_{STAT}$) was twice as variable as the maximum recoil pressure (RP) (15.7%, 8.1% respectively).

The correlation coefficient for sternal length (STERNL) was poor ($r < 0.66$) but the only significant difference between repeated measurements was for chest depth (CHD; p < 0.05). However, the average difference between the measurements of chest depth was 4mm, or about 2%.

5.2 Longitudinal Study

5.2.1 Subjects

There were 269 young men recruited at the time of study into apprenticeships at British Shipbuilders and all were measured in the first survey. A total of 240 (89%) of these subjects returned for repeat measurements and 226 (84% of the original population) were seen in the third survey. There were 9 men who were not seen in the first survey so that a total of 217 men had data for all three years of the study (Fig 5.1). Excluded from these data were 14 men who reported respiratory symptoms at any visit during the study and 5 men who had missing, irretrievable data (Table 5.1). Consequently, 198 young male apprentices were included in the analysis with valid measurements on all three occasions during the study (the sample population).
FIG. 5.1  MEN SEEN IN LONGITUDINAL STUDY

First survey

Second survey

Third survey

20

23 217 9
<table>
<thead>
<tr>
<th>Number of Men</th>
<th>Reason for Exclusion from Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>History of Asthma</td>
</tr>
<tr>
<td>2</td>
<td>Cough and/or Phlegm for 3 months/year</td>
</tr>
<tr>
<td>4</td>
<td>Wheeze on most days/nights</td>
</tr>
<tr>
<td>2</td>
<td>Phlegm for 3 months/year + Asthma</td>
</tr>
<tr>
<td>1</td>
<td>Cough and Phlegm for 3 months/year + Wheeze</td>
</tr>
<tr>
<td>5</td>
<td>Missing/Irretrievable data</td>
</tr>
</tbody>
</table>

Total = 19
The mean interval between the first and second series of measurements was 13.7 months (SD 2.0). The mean interval between the second and third series of measurements was 14.0 months (SD 2.76).

5.2.2 Demographic Data

1) Job Categories

All the 198 young men in the study were residents of the Tyneside area with apprenticeships in heavy industry. Most of them were employed as electricians (24.7%) or platers (22.7%) with the remainder being welders (11.1%) and joiners (9.6%). This pattern was similar in the group of 71 men not included in the study, although it appears that a greater percentage of caulker-burners (15.5%) and shipwrights (15.5%) were found in this excluded population (Table 5.2).

2) Age

The method of sample selection from an age categorised group of apprentices ensured that both the sample and excluded populations had similar age profiles.

<table>
<thead>
<tr>
<th>Age at Entry (years)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Maximum</td>
<td>Minimum</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Sample population age</td>
<td>16.80</td>
<td>.28</td>
<td>17.64</td>
<td>16.23</td>
<td>198</td>
</tr>
<tr>
<td>Excluded population age</td>
<td>16.78</td>
<td>.29</td>
<td>17.28</td>
<td>16.23</td>
<td>71</td>
</tr>
</tbody>
</table>

There was no significant difference between these populations (Student's t-test, p > 0.05)
<table>
<thead>
<tr>
<th>Trade</th>
<th>Number In Sample Population</th>
<th>Number In Excluded Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caulker-Burner</td>
<td>12 (6.1%)</td>
<td>11 (15.5%)</td>
</tr>
<tr>
<td>Welder</td>
<td>22 (11.1%)</td>
<td>5 (7.0%)</td>
</tr>
<tr>
<td>Joiner</td>
<td>19 (9.6%)</td>
<td>4 (5.6%)</td>
</tr>
<tr>
<td>Draughtsman</td>
<td>11 (5.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Electrician</td>
<td>49 (24.7%)</td>
<td>16 (22.5%)</td>
</tr>
<tr>
<td>Rigger</td>
<td>1 (0.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Shipwright</td>
<td>11 (5.5%)</td>
<td>11 (15.5%)</td>
</tr>
<tr>
<td>Mechanical Technician</td>
<td>5 (2.5%)</td>
<td>4 (5.6%)</td>
</tr>
<tr>
<td>Fitter</td>
<td>10 (5.1%)</td>
<td>-</td>
</tr>
<tr>
<td>Plater</td>
<td>45 (22.7%)</td>
<td>11 (15.5%)</td>
</tr>
<tr>
<td>Coppersmith</td>
<td>6 (3.0%)</td>
<td>5 (7.0%)</td>
</tr>
<tr>
<td>Plumber</td>
<td>7 (3.5%)</td>
<td>4 (5.6%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>198</strong></td>
<td><strong>71</strong></td>
</tr>
</tbody>
</table>
3) Smoking History

There were 137 men in the sample population that were current non-smokers at the start of the study (69.2%); 8 were ex-smokers. There were 123 men who remained non-smokers throughout (89.8%) and 14 men began smoking at some time.

There were 61 men who were smokers at the beginning of the study (30.8% of the sample population). Thereafter 52 men continued to smoke throughout (85.2%) and their mean weekly consumption of cigarettes was 15 in the first survey, 21 in the second survey and 23 in the third survey. Two men changed their smoking habit from small cigars to manufactured cigarettes. The remaining 9 smokers (14.8%) at the start of the study stopped smoking at some time.

The group of 71 men excluded from the sample population had similar smoking histories when the study began. There were 43 men who were non-smokers (61%): 4 were ex-smokers. The remaining 28 men were smokers (39%) with a mean consumption of 18 cigarettes per day.

These results are summarised in Table 5.3.

4) Respiratory Symptoms

Over 90% of both the sample population and the group of 71 excluded men had no reported symptoms according to the MRC questionnaire. Only hay fever was reported in more than 10% of each population. (Table 5.4).

5.2.3 Investigating Possible Selection Bias

There were 198 men selected for the sample population leaving 71 men excluded from the study. They have already been shown to have similar demographic characteristics.

To determine whether selection bias occurred, the two groups were compared using Student’s t-test on all interval variables measured in the first survey. The only variable
### TABLE 5.3

**Smoking History - Longitudinal Study**

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>Number In Sample Population</th>
<th>Number In Excluded Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers throughout study</td>
<td>115 (58%)</td>
<td>39 (55%)</td>
</tr>
<tr>
<td>Ex-smokers throughout study</td>
<td>8 (4%)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Smokers throughout study</td>
<td>52 (26.3%)</td>
<td>28 (39%)</td>
</tr>
<tr>
<td>Started smoking in study</td>
<td>12 (6%)</td>
<td>-</td>
</tr>
<tr>
<td>Stopped smoking in study</td>
<td>7 (3.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Started then stopped smoking in study</td>
<td>2 (1%)</td>
<td>-</td>
</tr>
<tr>
<td>Stopped then started smoking in study</td>
<td>2 (1%)</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>198</td>
<td>71</td>
</tr>
</tbody>
</table>
### TABLE 5.4

**Respiratory Symptoms - Longitudinal Study**

<table>
<thead>
<tr>
<th>SYMPTOM - HISTORY (Have you ever suffered from?)</th>
<th>Sample Population</th>
<th>Excluded Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Chest Injury</td>
<td>2(1%)</td>
<td>196(99%)</td>
</tr>
<tr>
<td>Heart Trouble</td>
<td>1(0.5%)</td>
<td>197(99.5%)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>14(7.1%)</td>
<td>184(92.9%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3(1.5%)</td>
<td>195(98.5%)</td>
</tr>
<tr>
<td>Pleurisy</td>
<td>-</td>
<td>198(100%)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>-</td>
<td>198(100%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>-</td>
<td>198(100%)</td>
</tr>
<tr>
<td>Hay Fever</td>
<td>24(12.1%)</td>
<td>174(87.9%)</td>
</tr>
</tbody>
</table>
which was significantly different at the 5% level was residual volume (p = 0.033). (This result also occurred when residual volume was standardised using the allometric constant from the total population). The sample population had a smaller residual volume than the excluded population at the start of the study. This was investigated further to ensure that the change in residual volume during the study period was the same in each group although the initial values may have been statistically different.

The 71 men excluded from the study included 28 men who were measured in the third survey. At the end of the study the 28 men and the sample population had comparable residual volumes. There was no significant difference in the change in residual volume over the two years study period between the two study groups.

5.2.4 Anthropometric Data

The anthropometric dimensions increased during the study period 17-19 years (Table 5.5). These increases were significant at the 5% level using Student's t-test.

Over the age interval 17-18 years all the anthropometric dimensions increased significantly with the possible exception of chest depth (p = 0.053). Over the interval 18-19 years the majority of dimensions increased but the variables which reflected the length of the thorax did not change significantly. These include sitting height (p = 0.88), sternal height (p = 0.33) and right costal margin length (p = 0.08) (Table 5.6). Chest width and shoulder width showed more change between 18-19 years than 17-18 years, in contrast to the change in chest depth which occurred mainly in the 17-18 year old interval (Table 5.6).

Since the length of the thorax remained the same for individuals measured in the second and third surveys, the volume of the chest was assessed using the formula for the area of an ellipse (\( \pi ab \)). The radii a and b were calculated from the diameters of chest width and chest
TABLE 5.5
Anthropometric Data - Longitudinal Study

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>FIRST SURVEY</th>
<th></th>
<th></th>
<th></th>
<th>SECOND SURVEY</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>THIRD SURVEY</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Min</td>
<td>Max</td>
<td>Mean</td>
<td>SD</td>
<td>Min</td>
<td>Max</td>
<td>Mean</td>
<td>SD</td>
<td>Min</td>
<td>Max</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STAT (m)</td>
<td>1.74</td>
<td>0.07</td>
<td>1.49</td>
<td>1.88</td>
<td>1.76</td>
<td>0.07</td>
<td>1.57</td>
<td>1.89</td>
<td>1.77</td>
<td>0.07</td>
<td>1.57</td>
<td>1.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMASS (kg)</td>
<td>63.70</td>
<td>10.38</td>
<td>41.40</td>
<td>110.00</td>
<td>67.24</td>
<td>10.16</td>
<td>44.10</td>
<td>102.70</td>
<td>69.73</td>
<td>9.99</td>
<td>48.20</td>
<td>102.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTOS (m)</td>
<td>1.41</td>
<td>0.06</td>
<td>1.19</td>
<td>1.53</td>
<td>1.42</td>
<td>0.06</td>
<td>1.25</td>
<td>1.54</td>
<td>1.42</td>
<td>0.06</td>
<td>1.24</td>
<td>1.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SITHT (m)</td>
<td>1.53</td>
<td>0.04</td>
<td>1.39</td>
<td>1.72</td>
<td>1.55</td>
<td>0.04</td>
<td>1.43</td>
<td>1.63</td>
<td>1.55</td>
<td>0.03</td>
<td>1.45</td>
<td>1.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCML (cm)</td>
<td>29.64</td>
<td>2.06</td>
<td>23.30</td>
<td>35.70</td>
<td>31.20</td>
<td>1.90</td>
<td>25.40</td>
<td>36.50</td>
<td>31.38</td>
<td>1.88</td>
<td>24.90</td>
<td>36.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCML (cm)</td>
<td>29.03</td>
<td>1.94</td>
<td>23.30</td>
<td>35.50</td>
<td>31.07</td>
<td>1.88</td>
<td>25.50</td>
<td>36.50</td>
<td>31.19</td>
<td>1.77</td>
<td>24.90</td>
<td>36.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STERNL (cm)</td>
<td>17.33</td>
<td>1.55</td>
<td>13.50</td>
<td>21.70</td>
<td>20.11</td>
<td>1.70</td>
<td>15.70</td>
<td>25.20</td>
<td>20.19</td>
<td>1.69</td>
<td>15.40</td>
<td>24.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHW (cm)</td>
<td>38.02</td>
<td>2.52</td>
<td>25.50</td>
<td>43.00</td>
<td>38.86</td>
<td>2.33</td>
<td>27.30</td>
<td>44.80</td>
<td>39.51</td>
<td>2.06</td>
<td>34.50</td>
<td>44.70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**TABLE 5.5 (continued)**

**Anthropometric Data - Longitudinal Study**

| VARIABLE | FIRST SURVEY | | | | SECOND SURVEY | | | | | | THIRD SURVEY | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | |
| HIPW (cm) | 27.00 | 1.70 | 22.60 | 32.00 | 27.42 | 1.69 | 22.90 | 31.80 | 27.76 | 1.64 | 23.20 | 32.70 |
| CHW (cm) | 26.26 | 2.18 | 15.90 | 30.80 | 26.99 | 1.97 | 18.90 | 31.80 | 28.12 | 1.81 | 24.20 | 32.90 |
| CHD (cm) | 18.72 | 2.12 | 13.70 | 29.80 | 18.96 | 1.83 | 14.10 | 25.60 | 19.32 | 1.82 | 15.20 | 28.50 |
| FAT % | 10.19 | 4.30 | 3.59 | 27.92 | 12.80 | 4.94 | 4.84 | 31.37 | 13.59 | 4.65 | 4.96 | 30.13 |
| FFM (kg) | 56.89 | 7.25 | 39.16 | 79.45 | 58.28 | 6.65 | 41.00 | 77.53 | 59.94 | 6.62 | 43.62 | 76.39 |
TABLE 5.6
Changes in Anthropometric Variables - Longitudinal Study

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>Mean Change</th>
<th>Apportionment (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st-3rd Survey</td>
<td>1st-2nd Survey</td>
</tr>
<tr>
<td>STATURE (m)</td>
<td>0.03</td>
<td>82.2</td>
</tr>
<tr>
<td>BMASS (kg)</td>
<td>6.03</td>
<td>62.3</td>
</tr>
<tr>
<td>FTOS (m)</td>
<td>0.02</td>
<td>71.5</td>
</tr>
<tr>
<td>SITHT (cm)</td>
<td>2.10</td>
<td>92.3</td>
</tr>
<tr>
<td>LCML (cm)</td>
<td>1.73</td>
<td>98.0</td>
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<tr>
<td>RCML (cm)</td>
<td>2.16</td>
<td>95.6</td>
</tr>
<tr>
<td>STERNL (cm)</td>
<td>2.86</td>
<td>99.0</td>
</tr>
<tr>
<td>SHW (cm)</td>
<td>1.48</td>
<td>31.5</td>
</tr>
<tr>
<td>HIPW (cm)</td>
<td>0.76</td>
<td>49.2</td>
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<tr>
<td>CHW (cm)</td>
<td>1.86</td>
<td>25.0</td>
</tr>
<tr>
<td>CHD (cm)</td>
<td>0.60</td>
<td>64.8</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>3.05</td>
<td>91.8</td>
</tr>
</tbody>
</table>

* expressed as Yearly internal change x 100(%)  
Change over study

NS - not significant
depth. (This volume could not be calculated for the first survey as chest lengths increased significantly between the first and second surveys and the area of an ellipse would not be appropriate).

There was a significant increase in chest volume between the ages 18-19 years equivalent to a 6.1% change in volume.

5.2.5 Lung Volume Data

The lung volumes increased significantly over the study period (Table 5.7).

Over the age interval 17-18 years residual volume remained constant although between 18-19 years there was a significant increase. The pattern of change over the study period was reflected in the percentage attributed to each yearly interval (Table 5.8).

The functional residual capacity increased by 5.63% during the 18-19 year interval, a similar value to that of chest volume during this period (6.1%).

5.2.6 Respiratory Pressure Data

The respiratory pressure measurements were available for the second and third surveys.

<table>
<thead>
<tr>
<th>Maximal expiratory pressure</th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(MEP; kPa)</td>
<td>13.32</td>
<td>3.44</td>
<td>12.76</td>
<td>2.68</td>
</tr>
<tr>
<td>Maximal inspiratory pressure</td>
<td>10.42</td>
<td>3.01</td>
<td>11.10</td>
<td>3.18</td>
</tr>
<tr>
<td>(MIP; kPa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The decrease in maximal expiratory pressure and the increase in maximal inspiratory pressure were both significant during this interval (p < 0.05). The changes expressed as a
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>FIRST SURVEY</th>
<th></th>
<th>SECOND SURVEY</th>
<th></th>
<th>THIRD SURVEY</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Min</td>
<td>Max</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>TLC (1)</td>
<td>6.05</td>
<td>0.94</td>
<td>3.79</td>
<td>8.94</td>
<td>6.33</td>
<td>0.87</td>
</tr>
<tr>
<td>FRC (1)</td>
<td>2.79</td>
<td>0.59</td>
<td>1.37</td>
<td>4.38</td>
<td>2.98</td>
<td>0.58</td>
</tr>
<tr>
<td>RV (1)</td>
<td>0.99</td>
<td>0.28</td>
<td>0.43</td>
<td>1.89</td>
<td>1.02</td>
<td>0.33</td>
</tr>
<tr>
<td>ERV (1)</td>
<td>1.80</td>
<td>0.42</td>
<td>0.84</td>
<td>2.86</td>
<td>1.96</td>
<td>0.38</td>
</tr>
<tr>
<td>EVC (1)</td>
<td>4.91</td>
<td>0.74</td>
<td>2.70</td>
<td>6.87</td>
<td>5.21</td>
<td>0.71</td>
</tr>
<tr>
<td>IVC (1)</td>
<td>4.90</td>
<td>0.75</td>
<td>2.62</td>
<td>6.90</td>
<td>5.18</td>
<td>0.71</td>
</tr>
<tr>
<td>IC (1)</td>
<td>3.26</td>
<td>0.60</td>
<td>1.79</td>
<td>5.25</td>
<td>3.34</td>
<td>0.55</td>
</tr>
</tbody>
</table>
TABLE 5.8

Changes in Lung Volume Measurements - Longitudinal Study

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>Mean Change</th>
<th>Apportionment (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st-3rd Survey</td>
<td>1st-2nd Survey</td>
</tr>
<tr>
<td>TLC (1)</td>
<td>0.44</td>
<td>53.4</td>
</tr>
<tr>
<td>FRC (1)</td>
<td>0.36</td>
<td>65.3</td>
</tr>
<tr>
<td>RV (1)</td>
<td>0.11</td>
<td>50.4</td>
</tr>
<tr>
<td>ERV (1)</td>
<td>0.25</td>
<td>84.1</td>
</tr>
<tr>
<td>EVC (1)</td>
<td>0.40</td>
<td>72.1</td>
</tr>
<tr>
<td>IC (1)</td>
<td>0.09</td>
<td>79.3</td>
</tr>
</tbody>
</table>

* expressed as *Yearly interval change* x 100(%)  
Change over study

NS - not significant
percentage were 3.25% and -6.40% respectively. These results
demonstrate a twofold change in inspiratory respiratory pressure
compared with expiratory respiratory pressure during the same
period of development.

5.2.7 Correlations and Associations

The change in residual volume over the period 18-19 years was not
significantly correlated with the change that occurred in any of
the thoracic dimensions or variables reflecting the length of the
body, including stature. The change in chest volume by assessing
the coronal area was positively correlated with the change in both
stature and vital capacity. This was also true for chest width.
Both the changes in chest width and chest depth were significantly
and positively correlated with the change in inspiratory capacity,
a relationship which was strengthened when they were combined to
give chest volume.

The change in chest depth during the period 18-19 years was not
related to the change in stature.

These results are summarised in Table 5.9.

When the second series of measurements were obtained, chest
volume, chest width and chest depth were positively and
significantly correlated with all lung volumes except residual
volume. These variables were also highly correlated with stature
and expiratory and inspiratory maximal respiratory pressure.

At the end of the study, the thoracic dimensions and chest volume
were still highly correlated with stature. However, the pattern
of association between these variables and the lung volumes had
changed. Residual capacity, functional residual capacity and
expiratory reserve volume were not correlated with chest depth,
although chest width was highly correlated with all lung volumes.
The maximal respiratory pressures remained highly correlated with
the thoracic dimensions and chest volume.
TABLE 5.9
Correlation Matrix for Changes in Variables between Second and Third Surveys
Longitudinal Study

<table>
<thead>
<tr>
<th></th>
<th>STAT</th>
<th>TLC</th>
<th>FRC</th>
<th>RV</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
<th>MEP</th>
<th>MIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHW</td>
<td>1.000</td>
<td>0.228</td>
<td>-0.078</td>
<td>0.047</td>
<td>-0.126</td>
<td>0.258</td>
<td>0.209</td>
<td>0.003</td>
<td>-0.011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>CHD</td>
<td>0.112</td>
<td>0.018</td>
<td>-0.222</td>
<td>-0.065</td>
<td>-0.205</td>
<td>0.085</td>
<td>0.275</td>
<td>-0.001</td>
<td>0.071</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>CHVOL</td>
<td>0.198</td>
<td>0.056</td>
<td>-0.226</td>
<td>-0.028</td>
<td>-0.238</td>
<td>0.188</td>
<td>0.320</td>
<td>0.003</td>
<td>0.056</td>
</tr>
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<tr>
<td>STAT</td>
<td>1.000</td>
<td>0.344</td>
<td>0.177</td>
<td>0.084</td>
<td>0.142</td>
<td>0.403</td>
<td>0.177</td>
<td>-0.073</td>
<td>0.086</td>
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<tr>
<td>MIP</td>
<td>0.086</td>
<td>0.060</td>
<td>-0.032</td>
<td>0.029</td>
<td>-0.058</td>
<td>0.061</td>
<td>0.103</td>
<td>0.179</td>
<td>1.000</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MEP</td>
<td>-0.073</td>
<td>-0.047</td>
<td>-0.078</td>
<td>-0.101</td>
<td>-0.019</td>
<td>0.089</td>
<td>0.038</td>
<td>1.000</td>
<td>0.179</td>
</tr>
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<tr>
<td>SITH</td>
<td>0.543</td>
<td>0.284</td>
<td>0.140</td>
<td>0.038</td>
<td>0.130</td>
<td>0.316</td>
<td>0.153</td>
<td>0.072</td>
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</tr>
<tr>
<td>STERNL</td>
<td>0.258</td>
<td>0.183</td>
<td>0.141</td>
<td>0.132</td>
<td>0.064</td>
<td>0.159</td>
<td>0.041</td>
<td>0.094</td>
<td>0.028</td>
</tr>
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<td>*</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>RCML</td>
<td>0.354</td>
<td>0.182</td>
<td>0.070</td>
<td>0.050</td>
<td>0.043</td>
<td>0.212</td>
<td>0.123</td>
<td>0.082</td>
<td>-0.012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Significant p < 0.05
These results are summarised in Tables 5.10 and 5.11.

5.2.8 Regression Analysis

The results from the third survey, at the end of the longitudinal study, were analysed to give linear regression equations for each lung volume (l) based on stature (m). These gave the following:

\[
\begin{align*}
\text{TLC} &= 7.93 \text{ (STATURE)} - 7.49 \quad \text{SE} \pm 0.62 \quad R^2 = 0.443 \\
\text{FRC} &= 4.30 \text{ (STATURE)} - 4.43 \quad \text{SE} \pm 0.51 \quad R^2 = 0.255 \\
\text{RV} &= 1.68 \text{ (STATURE)} - 1.86 \quad \text{SE} \pm 0.29 \quad R^2 = 0.133 \\
\text{ERV} &= 2.64 \text{ (STATURE)} - 2.61 \quad \text{SE} \pm 0.37 \quad R^2 = 0.195 \\
\text{EVC} &= 6.26 \text{ (STATURE)} - 5.73 \quad \text{SE} \pm 0.53 \quad R^2 = 0.399 \\
\text{IC} &= 3.63 \text{ (STATURE)} - 3.06 \quad \text{SE} \pm 0.47 \quad R^2 = 0.222
\end{align*}
\]

The residual values were obtained by taking the difference between the observed lung volumes and those predicted by the above equations based on stature. These residual values were then correlated with the thoracic dimensions and chest volume (Table 5.12). The results show that the prediction of total lung capacity, expiratory vital capacity and inspiratory capacity would be less variable if chest depth and chest width were included in the linear regression. However, the prediction of residual volume and functional residual capacity would not be helped by the addition of these variables to the regression equations.

The results from the forward stepwise linear regression analysis are given in Table 5.13. The inclusion of stature reduced the variance of the total lung capacity and expiratory vital capacity equations more than the thoracic dimensions. Chest width, however, reduced the variance of the inspiratory capacity regression equation more than stature. Chest depth significantly contributed to the prediction of expiratory vital capacity and inspiratory capacity but not total lung capacity.
TABLE 5.10

Correlation Coefficient Matrix between Variables Measured in the First Survey-Longitudinal Study

<table>
<thead>
<tr>
<th></th>
<th>STAT</th>
<th>TLC</th>
<th>FRC</th>
<th>RV</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
<th>MEP</th>
<th>MIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHW</td>
<td>0.342</td>
<td>0.509</td>
<td>0.253</td>
<td>0.128</td>
<td>0.274</td>
<td>0.575</td>
<td>0.539</td>
<td>0.219</td>
<td>0.172</td>
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<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
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</tr>
<tr>
<td>CHD</td>
<td>0.243</td>
<td>0.363</td>
<td>0.134</td>
<td>0.033</td>
<td>0.175</td>
<td>0.435</td>
<td>0.432</td>
<td>0.199</td>
<td>0.176</td>
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<td></td>
<td>*</td>
<td>*</td>
<td>(p=0.06)</td>
<td>*</td>
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<tr>
<td>CHVOL</td>
<td>0.342</td>
<td>0.517</td>
<td>0.219</td>
<td>0.082</td>
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<td>0.604</td>
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<tr>
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<td>0.625</td>
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<tr>
<td>MIP</td>
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<td>0.004</td>
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<td>*</td>
<td>(-)</td>
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<td>MEP</td>
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<td>0.084</td>
<td>-0.099</td>
<td>-0.194</td>
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<td>0.201</td>
<td>0.237</td>
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<td>(-)</td>
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<tr>
<td>SITHT</td>
<td>0.767</td>
<td>0.663</td>
<td>0.501</td>
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<td>0.639</td>
<td>0.520</td>
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<td>*</td>
<td>*</td>
<td>*</td>
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</tr>
<tr>
<td>STERNL</td>
<td>0.502</td>
<td>0.519</td>
<td>0.358</td>
<td>0.239</td>
<td>0.340</td>
<td>0.519</td>
<td>0.444</td>
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</table>

* Significant p < 0.05
### TABLE 5.11

Correlation Coefficient Matrix between Variables Measured in the Second Survey-Longitudinal Study

<table>
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<th>STAT</th>
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<th>RV</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
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<th>MIP</th>
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* Significant p < 0.05
TABLE 5.12
Correlation Coefficient Matrix, between the Residual Values of the Regression Analysis and the Thoracic Dimensions in the Third survey-Longitudinal Study

<table>
<thead>
<tr>
<th>RESIDUALS</th>
<th>TLC</th>
<th>FRC</th>
<th>RV</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
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</thead>
<tbody>
<tr>
<td>CHW</td>
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<td>-.067</td>
<td>-.016</td>
<td>.010</td>
<td>.386</td>
<td>.416</td>
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<tr>
<td>CHD</td>
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<td>-.002</td>
<td>-.079</td>
<td>-.031</td>
<td>.302</td>
<td>.340</td>
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<td>CHVOL</td>
<td>.299</td>
<td>-.060</td>
<td>-.060</td>
<td>-.031</td>
<td>.406</td>
<td>.458</td>
</tr>
</tbody>
</table>

* Significant p < 0.05
TABLE 5.13

Results of The Forward Stepwise Linear Regression Analysis-Longitudinal Study

Total Lung Capacity

\[ TLC = 6.47 \text{(STAT)} + 0.13 \text{(CHW)} - 8.606 \text{ SE} + 0.58 \]

**Reduction in Variance**

- Stepwise \( R^2 = 44.26\% \) CHW contributes 6.52%
- \( R^2 = 50.78\% \)

Expiratory Vital Capacity

\[ EVC = 4.53 \text{(STAT)} + 0.12 \text{(CHW)} + 0.065 \text{(CHD)} - 7.321 \text{ SE} + 0.47 \]

**Reduction in Variance**

- Stepwise \( R^2 = 39.96\% \) CHW contributes 10.68%
- \( R^2 = 50.64\% \) CHD contributes 2.44%
- \( R^2 = 53.08\% \)

Inspiratory Capacity

\[ IC = 0.11 \text{(CHW)} + 1.97 \text{(STAT)} + 0.066 \text{(CHD)} - 4.60 \text{ SE} + 0.40 \]

**Reduction in Variance**

- Stepwise \( R^2 = 32.37\% \) STAT contributes 5.97%
- \( R^2 = 38.34\% \) CHD contributes 4.27%
- \( R^2 = 42.61\% \)

(STAT (m); CHD (cm); CHW (cm))
5.3 Cross-sectional Study

5.3.1. Subjects

There were 198 men seen in the third survey of the longitudinal study at age 19 years. The aim was to select two distinct sample groups from these men for the cross-sectional study; one group of men having large lung volumes and the other group having relatively small lung volumes for their height.

The regression equation to predict total lung capacity based on stature at the end of the longitudinal study was:

\[ TLC = 7.93 \text{ (stature)} - 7.49 \]

and one standard deviation unit of the equation was equivalent to 0.62 litres. In order to obtain the extreme 20% of the population with greater than predicted total lung capacity, and the extreme 20% with less than predicted total lung capacity, a standard deviate of 0.843 was required (Fig 5.2). In this context, where the standard deviation of the equation is equivalent to 0.62 litres, a standard deviate of 0.843 gives the extreme 40% of the population (20% above, 20% below) if:

\[ \text{Actual TLC} = \text{Predicted TLC} \pm 0.5227 \text{ litres} \]

This was applied to the third survey longitudinal data and selected 85 men for the cross-sectional study.

Out of 85 men selected, 63 volunteered and agreed to attend the two appointments in the study. There were 9 men rejected (6 with missing data and 3 with technically unsatisfactory lung compliance data). These 9 men, together with the 22 men who refused to attend, were the excluded population. A total of 54 men were included in the cross-sectional study analysis, (the sample population) 27 had greater than predicted total lung capacity and 27 had lower than predicted total lung capacity.
FIG. 5.2 SELECTION OF MEN FOR CROSS-SECTIONAL STUDY

No. of men (n=198)

20% 0.84

SD

n=42

0.521
n=43

20%

SD

n=42

n=27

SMALL TLC GROUP

LARGE TLC GROUP
All the men were seen in the cross-sectional study. The time interval between their measurements in the third survey of the longitudinal study and their visit to the laboratory for the cross-sectional study averaged 16.96 months (SD 2.75) for those with large TLC and 16.22 months (SD 2.45) for those with small TLC. The men were also required to visit Wallsend Chest Clinic for the chest X-rays to be taken in the cross-sectional study. Each subject attended the chest clinic within 5 months of the laboratory visit, the mean interval between these visits being 1.2 months (SD 0.9) for the men with large TLC and 1.7 months (SD 1.5) for the men with small TLC.

5.3.2. Demographic Data

1) Job Categories

Most men in both sample groups were electricians and platers with more electricians being excluded from the large TLC sample group and more platers being excluded from the small TLC sample group (Table 5.14).

2) Smoking History

Most men in both sample groups were non-smokers representing similar proportions in each sample population (Table 5.15). Those men who were smokers had a cigarette consumption of 20-26 cigarettes per week.

3) Physical Activity

Over 65% of all the selected and excluded groups reported taking part in regular sporting activity; the majority of these men considered their sport as competitive training. In this respect all groups were comparable, less than a third in each group reported no regular exercise (Table 5.16).
### TABLE 5.14

**Job Categories - Cross-sectional Study**

<table>
<thead>
<tr>
<th></th>
<th>SMALL TLC</th>
<th></th>
<th>LARGE TLC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sample</td>
<td>Excluded</td>
<td>Sample</td>
<td>Excluded</td>
</tr>
<tr>
<td></td>
<td>Group(n=27)</td>
<td>Group(n=15)</td>
<td>Group(n=27)</td>
<td>Group(n=16)</td>
</tr>
<tr>
<td>CAULKNER-BURNER</td>
<td>2</td>
<td>1</td>
<td>2</td>
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<tr>
<td>WELDER</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>DRAUGHTSMAN</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ELECTRICIAN</td>
<td>7</td>
<td>2</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>PLATER</td>
<td>10</td>
<td>5</td>
<td>8</td>
<td>1</td>
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<tr>
<td>SHIPWRIGHT</td>
<td></td>
<td></td>
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<td>1</td>
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<tr>
<td>COPPERSMITH</td>
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<td>FITTER</td>
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<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PLUMBER</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>JOINER</td>
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<td>3</td>
<td>3</td>
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</tbody>
</table>
TABLE 5.15

Smoking Histories - Cross-sectional Study

<table>
<thead>
<tr>
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<tbody>
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<td></td>
<td>Sample</td>
<td>Excluded</td>
<td>Sample</td>
<td>Excluded</td>
</tr>
<tr>
<td></td>
<td>Group(n=27)</td>
<td>Group(n=15)</td>
<td>Group(n=27)</td>
<td>Group(n=16)</td>
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<td>2</td>
<td>8</td>
<td>8</td>
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<td>NON-SMOKERS</td>
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<td>18</td>
<td>6</td>
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<td>EX-SMOKERS</td>
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<td>-</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>SMALL TLC</td>
<td></td>
<td>LARGE TLC</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>--------------</td>
<td>-----------</td>
<td>--------------</td>
</tr>
<tr>
<td></td>
<td>Sample(n=27)</td>
<td>Excluded Group(n=15)</td>
<td>Sample(n=27)</td>
<td>Excluded Group(n=16)</td>
</tr>
<tr>
<td>Regular Exercise (Competitive)</td>
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<td>5</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Regular Exercise (Non-competitive)</td>
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<td>3</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>No Exercise</td>
<td>13</td>
<td>7</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>
4) Respiratory Symptoms

In the third survey in the longitudinal study most of the 85 men selected for the cross-sectional study reported no history of respiratory symptoms (Table 5.17). Within and across the sample and excluded groups the most reported symptoms were a history of hay fever and bronchitis. However, no current cough or phlegm production for 3 months in a year were reported at the time of the survey.

5.3.3 Investigating Selection Bias

There were 27 men included in each of the two sample groups for the cross-sectional study. The 16 men who had been excluded from the sample group with large TLCs were compared with the 27 men who represented this group. Similarly, the 15 men who had been excluded from the sample groups with small TLCs were compared with the 27 men who represented this group. All men had been measured in the third survey of the longitudinal study. Student's t-test was applied to the anthropometric and lung volume variables. No significant difference between the excluded men and the sample population was found for any variable (p > 0.05).

5.3.4 Comparison between the Selected Sample Groups

Comparison was made between the two sample populations in the cross-sectional study. (The 27 men who had larger than predicted lung volumes were compared with the 27 men who had smaller than predicted lung volumes).

1) Anthropometric Measurements

There was no significant difference between the groups for most of the anthropometric variables measured in the longitudinal study (Table 5.18). The group with the larger lung volumes did have greater chest width and sitting height measurements; the difference being significant at the 5% level (p < 0.05). The 27 men in each group were of similar age, stature and weight at the time of the cross-sectional survey (Table 5.20).
TABLE 5.17
Respiratory Symptoms - Cross-sectional Study

<table>
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<th>SYMPTOM/PRESENT</th>
<th>SMALL TLC</th>
<th>LARGE TLC</th>
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<tr>
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<td>Sample Group (n=27)</td>
<td>Excluded Group (n=15)</td>
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<td>YES 2 NO 25</td>
<td>YES - NO 15</td>
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<tr>
<td>Heart Trouble</td>
<td>YES 27 NO -</td>
<td>YES - NO 15</td>
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<tr>
<td>Bronchitis</td>
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<td>YES 1 NO 14</td>
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<td>Pneumonia</td>
<td>YES 27 NO -</td>
<td>YES - NO 15</td>
</tr>
<tr>
<td>Pleurisy</td>
<td>YES 2 NO 25</td>
<td>YES - NO 15</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>YES 27 NO -</td>
<td>YES - NO 15</td>
</tr>
<tr>
<td>Asthma</td>
<td>YES 27 NO -</td>
<td>YES - NO 15</td>
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<td>Hay Fever</td>
<td>YES 3 NO 24</td>
<td>YES 2 NO 13</td>
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<td>VARIABLE (1982)</td>
<td>SMALL TLC GROUP (mean)</td>
<td>LARGE TLC GROUP (mean)</td>
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<td>------------------------</td>
<td>------------------------</td>
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<tr>
<td>STAT (m)</td>
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<td>1.78</td>
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<td>BMASS (kg)</td>
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<td>SITHT (m)</td>
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<td>1.57</td>
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<td>LCML (cm)</td>
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<td>31.84</td>
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<td>20.14</td>
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<td>HIPW (cm)</td>
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<td>CHW (cm)</td>
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<td>19.70</td>
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<tr>
<td>FFM (kg)</td>
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<td>61.99</td>
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</table>
2) Lung Volume Measurements

All the lung volume subdivisions of TLC were significantly greater, when measured in the third survey of the longitudinal study, in the group selected as having greater than predicted TLC (Table 5.19). These differences remained apparent when the lung volumes were measured again in the cross-sectional study (Table 5.20).

3) Respiratory Pressures

The maximal respiratory pressures measured in the third survey of the longitudinal study were not significantly different between the groups and they were similar when measured again in the cross-sectional study.

4) Pressure-Volume Curve Measurements

The results of the lung compliance measurements are given in Table 5.21. There was a significant difference between the two sample groups for inspiratory and expiratory lung compliance expressed as l.kPa^-1 (C_INS; C_EXP). When this was standardised for the size of the lung, the specific compliance (C_EXPTLC; C_INSTLC), taken from the expiratory pressure-volume curves, remained significantly different between the two sample groups. The specific compliance measurements taken from the inspiratory pressure-volume curves, however, were similar.

The replotted pressure-volume curves, from which compliance was measured and expressed as %TLC.kPa^-1 (C_ETLC, C_ITLC), also showed that the expiratory compliance was significantly greater in those men with larger lung volumes. However, no difference between the groups was found using compliance from the replotted inspiratory pressure-volume curves.

The recoil pressure results are given in Table 5.21. There was no significant difference between the two sample groups in the measurements of maximum recoil pressure at TLC (RP), recoil at TLC - 20%VC (P_STAT) or recoil at FRC (E_FRC, I_FRC) (p > 0.05).
TABLE 5.19

Comparison of Lung Volume Variables between the Two Groups - Longitudinal Study

<table>
<thead>
<tr>
<th>VARIABLE (1982)</th>
<th>SMALL TLC GROUP</th>
<th>LARGE TLC GROUP</th>
<th>STUDENT'S T-TEST</th>
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<tr>
<td></td>
<td>t value</td>
<td>p value</td>
<td></td>
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<tr>
<td>TLC (1)</td>
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<td>-10.77</td>
</tr>
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<td>FRC (1)</td>
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<td>3.67</td>
<td>- 5.83</td>
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<tr>
<td>RV (1)</td>
<td>0.95</td>
<td>1.37</td>
<td>-4.74</td>
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<tr>
<td>ERV (1)</td>
<td>1.84</td>
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<td>-4.64</td>
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<td>EVC (1)</td>
<td>4.80</td>
<td>6.01</td>
<td>-8.24</td>
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<tr>
<td>IC (1)</td>
<td>2.99</td>
<td>3.83</td>
<td>-6.02</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>16.35</td>
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<td>-1.56</td>
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<tr>
<td>FRC/TLC(%)</td>
<td>48.12</td>
<td>48.77</td>
<td>0.36</td>
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</table>
### TABLE 5.20

Results of Variables Measured in Cross-sectional Study

<table>
<thead>
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<th>VARIABLE (1983)</th>
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<th>LARGE TLC GROUP</th>
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</thead>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>AGE (yr)</td>
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</tr>
<tr>
<td>STAT (m)</td>
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<td>0.05</td>
</tr>
<tr>
<td>BMISS (kg)</td>
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</tr>
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</tr>
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<td>FRC (l)</td>
<td>3.33</td>
<td>0.93</td>
</tr>
<tr>
<td>ERV (l)</td>
<td>1.62</td>
<td>0.36</td>
</tr>
<tr>
<td>EVC (l)</td>
<td>4.59</td>
<td>0.56</td>
</tr>
<tr>
<td>IC (l)</td>
<td>2.97</td>
<td>0.51</td>
</tr>
<tr>
<td>MEP (kPa)</td>
<td>10.89</td>
<td>3.64</td>
</tr>
<tr>
<td>MIP (kPa)</td>
<td>11.89</td>
<td>3.05</td>
</tr>
</tbody>
</table>
# TABLE 5.21

**Pressure-Volume Curve Results - Cross-Sectional Study**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>SMALL TLC GROUP (mean)</th>
<th>LARGE TLC GROUP (mean)</th>
<th>STUDENT'S T-TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{EXP}}(\text{1.kPa}^{-1})$</td>
<td>1.77</td>
<td>2.72</td>
<td>- 5.40</td>
</tr>
<tr>
<td>$C_{\text{INS}}(\text{1.kPa}^{-1})$</td>
<td>1.56</td>
<td>2.14</td>
<td>- 4.01</td>
</tr>
<tr>
<td>$P_{\text{STAT}}\ (\text{kPa})$</td>
<td>1.24</td>
<td>1.23</td>
<td>0.14</td>
</tr>
<tr>
<td>$R_{\text{P}}\ (\text{kPa})$</td>
<td>3.75</td>
<td>3.72</td>
<td>0.12</td>
</tr>
<tr>
<td>$C_{\text{EXPTLC}}(\text{1.kPa}^{-1}.\text{TLC}^{-1})$</td>
<td>0.28</td>
<td>0.35</td>
<td>- 2.81</td>
</tr>
<tr>
<td>$C_{\text{INSTLC}}(\text{1.kPa}^{-1}.\text{TLC}^{-1})$</td>
<td>0.25</td>
<td>0.28</td>
<td>- 1.47</td>
</tr>
<tr>
<td>$C_{\text{ETLC}}(%\text{TLC.kPa}^{-1})$</td>
<td>28.65</td>
<td>36.09</td>
<td>- 2.99</td>
</tr>
<tr>
<td>$C_{\text{ITLC}}(%\text{TLC.kPa}^{-1})$</td>
<td>24.29</td>
<td>27.23</td>
<td>- 1.39</td>
</tr>
<tr>
<td>$E_{\text{FRC}}\ (\text{kPa})$</td>
<td>0.48</td>
<td>0.41</td>
<td>0.97</td>
</tr>
<tr>
<td>$I_{\text{FRC}}\ (\text{kPa})$</td>
<td>0.77</td>
<td>0.72</td>
<td>0.60</td>
</tr>
</tbody>
</table>
5) Tracheal Measurements

The two sample groups had similar lateral and posteroanterior diameters of the trachea. There were no significant difference between the two groups when these measurements were combined to give the tracheal cross-sectional area \((p > 0.05)\) (Table 5.22).

6) Respiratory Pressures

Maximal respiratory pressures were similar between the two groups. There were no significant differences between the expiratory or inspiratory maximal respiratory pressures (Table 5.22).

5.3.5 Correlations and Associations

These results are summarised in Table 5.23.

The lung compliance measurements from the pressure-volume curves were positively and significantly associated with all the volume subdivisions of the lung. However, this relationship disappeared when the lung compliance measurements were standardised for lung volume. The lung recoil pressures were unrelated to the lung volume measurements, with the exception of the recoil at FRC from the expiratory pressure-volume curves. This recoil pressure \((E_{FRC})\) was positively and significantly related to inspiratory capacity \((IC)\).

The tracheal diameters and cross-sectional area were not associated with the lung volume measurements, maximal respiratory pressures or pressure-volume curve variables. The maximal inspiratory pressure was positively correlated with the lung recoil pressure at TLC \((p < 0.05)\).

The longitudinal and cross-sectional study results are summarised in Tables 5.24 and 5.25 respectively.
TABLE 5.22
Tracheal Dimension and Respiratory Pressures Results
- Cross-sectional Study

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>SMALL TLC (mean)</th>
<th>LARGE TLC (mean)</th>
<th>STUDENT’S T-TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>t value</td>
</tr>
<tr>
<td>PTD (cm)</td>
<td>1.61</td>
<td>1.62</td>
<td>-0.18</td>
</tr>
<tr>
<td>LTD (cm)</td>
<td>1.59</td>
<td>1.54</td>
<td>1.20</td>
</tr>
<tr>
<td>XTRAC (cm²)</td>
<td>2.03</td>
<td>1.96</td>
<td>0.77</td>
</tr>
<tr>
<td>MIP (kPa)</td>
<td>11.99</td>
<td>12.26</td>
<td>-0.35</td>
</tr>
<tr>
<td>MEP (kPa)</td>
<td>10.89</td>
<td>10.36</td>
<td>-0.54</td>
</tr>
</tbody>
</table>
TABLE 5.23

Correlation Matrix between Variables
Total Cross-Sectional Study Population (n=54)

<table>
<thead>
<tr>
<th></th>
<th>TLC</th>
<th>FRC</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
<th>MEP</th>
<th>MIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_EXP</td>
<td>1.0</td>
<td>.491</td>
<td>.306</td>
<td>.376</td>
<td>.497</td>
<td>.443</td>
<td>.120</td>
</tr>
<tr>
<td></td>
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<td>*</td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_INS</td>
<td>1.0</td>
<td>.420</td>
<td>.301</td>
<td>.374</td>
<td>.398</td>
<td>.320</td>
<td>.179</td>
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<tr>
<td></td>
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<td></td>
<td>*</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_EXP_TLC</td>
<td>1.0</td>
<td>.097</td>
<td></td>
<td></td>
<td>.145</td>
<td>.196</td>
<td>.239</td>
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<td></td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_INS_TLC</td>
<td>1.0</td>
<td>-.020</td>
<td></td>
<td></td>
<td>.124</td>
<td>.053</td>
<td>.073</td>
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<td></td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_ETLC</td>
<td>1.0</td>
<td>.205</td>
<td>.099</td>
<td>.120</td>
<td>.180</td>
<td>.221</td>
<td>.169</td>
</tr>
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</tr>
<tr>
<td>C_ITLC</td>
<td>1.0</td>
<td>-.032</td>
<td></td>
<td></td>
<td>.036</td>
<td>.058</td>
<td>.131</td>
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<td></td>
</tr>
<tr>
<td>P_STAT</td>
<td>1.0</td>
<td>-.067</td>
<td>-.177</td>
<td></td>
<td>.069</td>
<td>.029</td>
<td>.130</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>1.0</td>
<td>-.071</td>
<td>-.099</td>
<td>-.103</td>
<td></td>
<td>.008</td>
<td>.030</td>
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<td></td>
</tr>
</tbody>
</table>

* Significant (p < 0.05)
TABLE 5.23 (continued)

Correlation Matrix between Variables
Total Cross-Sectional Study Population (n=54)

<table>
<thead>
<tr>
<th></th>
<th>TLC</th>
<th>FRC</th>
<th>ERV</th>
<th>EVC</th>
<th>IC</th>
<th>MEP</th>
<th>MIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>XTRAC (cm²)</td>
<td>.159</td>
<td>.204</td>
<td>.063</td>
<td>.064</td>
<td>.021</td>
<td>.018</td>
<td>-.138</td>
</tr>
<tr>
<td>PTD (cm)</td>
<td>.177</td>
<td>.182</td>
<td>.181</td>
<td>.125</td>
<td>.078</td>
<td>-.019</td>
<td>-.128</td>
</tr>
<tr>
<td>LTD (cm)</td>
<td>.103</td>
<td>.155</td>
<td>-.027</td>
<td>.019</td>
<td>-.014</td>
<td>.025</td>
<td>-.109</td>
</tr>
<tr>
<td>£FRC (kPa)</td>
<td>-.164</td>
<td>-.083</td>
<td>.159</td>
<td>-.160</td>
<td>-.426</td>
<td>*</td>
<td>-.083</td>
</tr>
<tr>
<td>IFRC (kPa)</td>
<td>-.052</td>
<td>.057</td>
<td>.211</td>
<td>-.012</td>
<td>-.202</td>
<td>.023</td>
<td>-.150</td>
</tr>
</tbody>
</table>

* Significant (p < 0.05)
<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>FIRST</th>
<th>SECOND</th>
<th>THIRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometry</td>
<td></td>
<td>increased</td>
<td></td>
</tr>
<tr>
<td>Chest Lengths</td>
<td>increased \</td>
<td>constant</td>
<td></td>
</tr>
<tr>
<td>Chest Width</td>
<td>increased \</td>
<td>increased (more so)</td>
<td></td>
</tr>
<tr>
<td>Chest Depth</td>
<td>increased \</td>
<td>increased (less so)</td>
<td></td>
</tr>
<tr>
<td>Lung Volumes</td>
<td></td>
<td>increased</td>
<td></td>
</tr>
<tr>
<td>IC</td>
<td>increased \</td>
<td>constant</td>
<td></td>
</tr>
<tr>
<td>VARIABLE</td>
<td>Small TLC Group vs Large TLC Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age/Stature</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung Volumes</td>
<td>Smaller</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Pressures</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung Recoil</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung Elasticity</td>
<td>Less compliant</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>More compliant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recoil at FRC</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tracheal Dimensions</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRC/TLC%</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV/TLC%</td>
<td>Similar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The population from which these results were obtained was young men training in shipbuilding trades. The results will strictly only apply to members of this specific group in heavy industry; however, there may be implications that extend to this age group in the general population.

Data have been obtained to assess the reproducibility of the methods used in this thesis. The procedure and results are given in Appendix 6. The elasticity measurements taken from inspiratory and expiratory pressure-volume curves were shown to be highly reproducible \( (r > 0.7) \), the most variable measurement being that of elastic recoil at TLC-20%VC \( (P_{STAT}) \) \( \Delta x / x = 15.1\% \). This may reflect the difficulty in assessing the exact pressure at which this lung volume was achieved. On the static pressure-volume curves, the volume of TLC-20%VC may have occurred when the shutter mechanism was in operation. This would have given a more accurate value for the pressure than if the shutter was open at this time. There was no way of standardising this procedure to ensure that the shutter mechanism was in operation on all occasions when the volume TLC-20%VC was achieved.

The anthropometric measurements of thoracic dimensions have been shown to be highly reproducible \( (r > 0.7, Appendix 6) \). The correlation coefficient for the repeated measurement of sternal length \( (STERNL, r=0.66) \) indicated that this is the most difficult thoracic dimension to repeat accurately. This may have been due to the difficulty in palpating the xiphoid process. There was no significant difference \( (p > 0.05) \) between the results on separate occasions for any of the thoracic dimensions with the exception of chest depth \( (CHD; p < 0.05) \). However, the difference averaged only 4mm or about 2% and the results indicated a greater change over the longitudinal study period (6cm).

In the present study, reproducibility of the lung volume and maximal respiratory pressures were not assessed as a direct procedure. However, repeated measurements of TLC \( (n=18) \), RV \( (n=20) \) and FRC \( (n=20) \) have been reported for subjects in the laboratory where this study was undertaken. (personal communication: Dr D J Chinn). The results have shown that the mean differences between measurements
were TLC (4.1%), RV (8%) and FRC (4.4%). The reported changes in the lung volumes in the present study were not, therefore, solely attributable to the variability of these measurements. The maximal respiratory pressures (MEP, MIP) have been reported to have average coefficients of variation of less than 10% in the laboratory where this present study was undertaken (personal communication: Dr D J Chinn). This was assessed in fourteen subjects who performed maximal respiratory pressures on two occasions with an interval of 14 days between repeated measurements.

The results of reproducibility assessments indicated that the procedures used in this study were valid. There was also no selection bias in the population under study. The sample population was shown to be representative of the original population (Section 5.3.3; Tables 5.2 - 5.4).

There were nine questions to be addressed as the basis of this research programme. These are discussed below and the implications of these findings given at the end of the chapter.

6.1 Can the increase in lung size be accounted for adequately by the increase in stature?

The 198 men in the longitudinal study proved to be a 'growing population' between the ages of 17-19 years. Their growth in stature was accompanied by an increase in all lung volume and anthropometric variables over the study period between 17-19 years. The percentage increase in lung volume over this period (7.49%), as given by total lung capacity, was greater than the percentage increase in stature (1.59%). This indicates that the lung volume change was relatively greater than the change in stature suggesting that lung growth exceeds that of somatic growth in this age group.

Most studies in the literature have concentrated on determining the age at which lung function begins to decline (57, 87, 94, 134). It is generally accepted that vital capacity continues to increase when height has stabilised, but the precise age at which this occurs is still a matter of controversy. Previous studies have not investigated the rate of lung growth just prior to the cessation of somatic growth. The present data have the advantage
of a large number of subjects having longitudinal measurements at a time when height was still increasing, before the adult value was attained. (The advantage of longitudinal surveys for this type of investigation has been discussed elsewhere (65)). The finding that lung growth exceeds somatic growth in the 17-19 year old age group is in contrast to results obtained from longitudinal studies at puberty. During the 'growth spurt' at puberty, the lung growth lags behind the increase in height (150). The authors explain that this is related to the growth of the thorax as the change in trunk length and chest depth also lag behind the change in stature. The present data suggest that this process may be reversed in later years; the thorax developing so that lung growth 'overtakes' the growth in stature and continues even when the adult height is reached. This is supported by the thoracic dimension results in the present study. Both chest width and chest depth increased during this period and may have contributed to the lung growth. The muscularity of the thorax and shoulder girdle have also been suggested as contributing factors to the increase in vital capacity when height remains constant (132); these may also effect lung volume in the age group 17-19 years. There are likely to be several factors that cause the greater rate of lung development compared to somatic growth during this period.

6.2 Do different subdivisions of the lung volume grow at the same rates?

Examining the lung volume changes between the first and third surveys in the longitudinal study, for the subdivisions of total lung capacity, there was a relatively greater change in the functional residual capacity (FRC) than the inspiratory capacity (IC) (Table 5.8). TLC was therefore affected more by a change in FRC than IC between the ages 17-19 years. The subdivisions of FRC, residual volume (RV) and expiratory reserve volume (ERV), appear to have a similar percentage increase during the study period. This suggests that RV and ERV contribute equally to the increase in functional residual capacity. It also suggests that the increase in the vital capacity was attributed mostly to the increase in expiratory reserve volume rather than inspiratory capacity. Since there was a relatively greater increase in FRC
than IC, the resting position of the lung, in terms of its volume, had changed during this period; the elastic forces within the thorax being "balanced" and at rest at a higher lung volume in the third survey. The calculation of the percentage increase in chest volume (6.1%) was comparable to the percentage increase in FRC during this study period (5.6%).

These results suggest a pattern of change in the subdivisions of total lung capacity during adolescence which has not been reported previously. Most longitudinal studies are designed to investigate the serial measurements of dynamic lung function tests. These studies do not include measurements of the static lung volumes. Dab has published a study which involved the measurement of TLC, FRC, RV, ERV and VC in two groups of male subjects with similar heights (43). However, the adolescent boys (16-22 years) were significantly taller than the children (12-15 years) at the 5% level and there were only 22 boys in the adolescent age group which makes interpretation of the results more difficult. It was reported that RV was smaller in the adolescents than in the children due to an increase in ERV and that TLC remains constant after puberty. The present study does not agree with these findings; the present data suggest that in the older age group all lung volumes, including TLC, were increasing and RV and ERV were increasing at the same rate. The differences in the interpretation of results in the adolescent age group may be due to measuring and selection differences between the two studies. In the present study the lung volume measurements were obtained annually in the same group of young men (Table 5.7). The sample size was much larger and the changes in lung volumes were unlikely to be affected by late puberty. A comparison of group ages 12-15 years and 16-22 years, with relatively few subjects in each age range, is likely to be affected by pubertal changes. These would have been reduced by obtaining developmental age. No doubt a more useful interpretation could have been achieved by using longitudinal measurements throughout the 12-22 year old age group. The present study was designed to provide some data in this way and be more informative than using age cohorts with cross-sectional measurements in the 12-22 year old age group.
Lung volumes and the standards recommended for their measurement have been extensively reviewed in the literature since the publication of the European Coal and Steel Community report in 1983 (ECSC report). Lung volumes may be measured by X-ray planimetry, helium dilution or body plethysmography techniques. Most authors agree that in healthy subjects the determination of total lung capacity is comparable by all three methods. The Resparameter Mk IV (P.K. Morgan Ltd) offered the advantage of being more portable and less expensive than the body plethysmograph in the situation where the equipment had to be moved between the four shipyards on the River Tyne, as in the present study. The helium dilution technique, if accurate calibration of the Resparameter is applied, also avoids the overestimation of the lung volumes that occurs with plethysmography. The Resparameter spirogram trace also gives the subdivisions of the total lung capacity that cannot be obtained from X-ray planimetry alone. The population in the present study was found to have lung volumes within the normal limits reported in a recent study of non-smoking adults. In this analysis the men were aged 15-91 years with only 17 subjects in each decade. There were relatively few subjects in the 17-19 year old age group compared with the present study. Also, the study reported results for non-smokers only which has been criticised as this leads to overestimating reference values. A comparison with other reference values suggests that the lung volume measurements for the present study are within normal ranges. It was therefore accepted that the study population was a healthy representation of the general population.

The ECSC report recommends the use of the inspiratory vital capacity to reflect the vital capacity of the subject. This is important as the residual volume is derived from the total lung capacity minus the vital capacity (RV-TLC-IVC). This recommendation assumes that in chronic airflow obstruction the vital capacity may be underestimated by the expiratory manoeuvre due to 'air-trapping'. Although it has been said that "FVC is usually greater than EVC and identical to IVC in normal subjects" (95), the present study found no significant difference between
the expiratory and inspiratory vital capacity measurements (p > 0.05). It is likely that in normal, healthy young men there is negligible airways obstruction and consequently all well performed vital capacity manoeuvres are equally valid.

6.3 Can the increase in lung size be attributed to an increase in the thoracic dimensions?

This was investigated using the results from the longitudinal study (Table 5.5). It was evident that during the ages 18-19 years the length of the thorax does not increase significantly. This suggests that any increase in lung volume during this period must be due to the increase in chest width and chest depth rather than any change in the length of the chest. Since the greatest proportion of change in chest width occurs between 18-19 years, in contrast to the relative change in chest depth, chest width should be the greatest determinant of the change in lung volume between 18-19 years (Table 5.6). The increase in chest width was correlated with the change in inspiratory capacity (IC). It was also significantly correlated with the increase in vital capacity. This was to be expected as inspiratory capacity is a component of vital capacity. Interestingly the change in functional residual capacity and total lung capacity were not correlated with the change in chest width. This indicates that there are factors which contribute to the change in TLC other than the increase in chest width during this period. This has important implications as the results from the present study have shown that the change in FRC was a major determinant of the change in TLC during this period. It was proposed that the resting level of the lung may have been altered due to changes in the elastic properties of the respiratory system; the cross-sectional study was designed to investigate these findings further.

The change in the thoracic dimensions may account for some of the change in the lung volumes during the study period. The importance of the thoracic dimensions in determining lung volumes was shown by the correlations between chest width, chest depth and subdivisions of total lung capacity (Tables 5.10 and 5.11). With the exception of residual volume, which may be influenced by
factors other than the change in thoracic dimensions, all the lung volumes were significantly correlated with chest width and chest depth in the first survey (Table 5.10). A year later in the second survey the chest width was significantly correlated with all lung volumes including residual volume (Table 5.11). This may be a reflection of the greater proportional increase in the chest width compared to the chest depth. In the third survey chest depth showed no significant correlation with functional residual capacity or its volume subdivisions (RV and ERV). These results indicate that the thoracic dimensions may contribute to the description of lung volumes in this age group. This has important implications for the derivation of normal reference values for static lung volumes if the addition of chest width and chest depth reduces the variance of the regression equations.

Thoracic dimensions have been used in the prediction of lung function indices in other studies but their use has been questioned as the measurements are so variable (27, 135). In the present study repeated measures were obtained in eleven subjects and sternum length was found to be the least reproducible (r=0.66), although the differences between the repeated measurements were not significant (p > 0.05). (The only significant difference between repeated measures was for chest depth where the average difference was 4mm, or about 2%). The variability of the sternum length measurement was most likely to be due to the difficulty in palpating the xiphoid process. It has been suggested that this is due to the transition of the xiphoid process from a fibrous plate to its ossified form (135). However, in the present study of men aged 17-19 years, the difficulty may have been due to the taut musculature over the area of palpation. The variability in the measurements of chest width and chest depth may be associated with the difficulties in standardising the procedure for measurement but the variables are useful in the prediction of lung function. The regression equations for the lung volumes in the third survey of the longitudinal study were calculated and the residual values correlated with the thoracic dimensions (Table 5.12). These results indicate that the unexplained variance of the prediction equations for TLC, EVC and IC based on stature should be reduced.
by the inclusion of chest width and chest depth in the analysis. Chest width appears to contribute more to the values of TLC, EVC and IC than chest depth (Table 5.13). This may reflect the greater proportional change associated with chest width during the 18-19 year old interval in the study period.

These results suggest that, during developmental phases where lung growth is not closely associated with change in stature, thoracic dimensions may improve the normal reference equations. This relationship may extend from puberty to the beginning of the decline in lung function associated with ageing. Chest volume can only be expressed as the area of an ellipse in a population where the length of the thorax is known to remain constant. It is, therefore, not a suitable reference variable for prediction equations, although it does combine chest width and chest depth.

6.4 Is the increase in chest volume due to lowering of the diaphragm?

The calculated increase in chest volume (6.1%) and the percentage increase in FRC (5.6%) were similar for the period 18-19 years. This suggests that the increase in chest volume accounted for a comparable increase in FRC. If the position of the diaphragm had altered to cause an increase in the chest volume then the increase in FRC would have been greater. It is, therefore, unlikely that significant lowering of the diaphragm occurred.

6.5 Is there a change in the lung elastic recoil associated with lung growth?

The study groups in the cross-sectional study had similar maximal recoil pressures measured at total lung capacity and TLC-20%VC ($P_{STAT}$; Table 5.21). At total lung capacity the recoil pressure is a combination of both chest wall and lung recoil as there is an increase in the inward recoil of the chest wall at full inspiration. At TLC-20%VC the recoil pressure is due to the recoil of the lung as the chest wall recoil is negligible at this volume. The two groups had similar recoil pressures at TLC-20%VC but for the group with the larger lung volumes this represents a lower lung recoil per unit of lung volume. This suggests that the men with larger lungs have less lung elastic recoil. A
reduction in lung elastic recoil should be associated with a
greater distensibility of the lung reflected in the results of
lung compliance. Indeed the lung compliance was significantly
different between the two groups for both expiratory and
inspiratory pressure-volume curves. The men with larger lungs
had a significantly greater lung compliance.

Lung compliance is correlated with the size of the lung and to
make comparisons between the two study groups the measurements
should be expressed in terms of lung volume (specific compliance
$C_{\text{EXP TLC}}$, $C_{\text{INST TLC}}$) to standardise for lung size (Table 5.21).
When this was calculated there was a significant difference
between the two groups for expiratory specific compliance
($p=0.007$) but no difference between them for inspiratory specific
compliance ($p=0.148$). To standardise for lung volume more
accurately the pressure-volume curves were replotted for each
subject using %TLC as the volume axis. Lung compliance was then
calculated as %TLC.kPa$^{-1}$ ($C_{\text{ETLC}}$, $C_{\text{ITLC}}$). The two groups had
significantly different results from the expiratory
pressure-volume curves ($p=0.017$) although the inspiratory
pressure-volume curves were similar ($p=0.146$). (This may be due
to the better reproducibility of the expiratory pressure-volume
curves which is discussed later in the text). These results
indicate that the group of men with large lung volumes had more
distensible lungs with less elastic recoil.

In the present study the elastic behaviour of the lungs has been
described as recoil pressure at various lung volumes. These have
been determined from pressure-volume curves where the
distensibility has been obtained and given as chord compliance.
The elasticity of the system can also be measured from
pressure-volume curves fitted with an exponential function - $V = V_{\text{max}} - Ae^{-Kp}$ (62). This was introduced to improve the description
of the pressure-volume curve (131). However, there is no
explanation why pressure-volume curves should be exponential in
nature (8). The function is established using $V_{\text{max}}$, the
extrapolated volume at which transpulmonary pressure is infinite,
which in normal healthy subjects has been shown to be similar to
total lung capacity (104% of TLC (34); 102.5% of TLC (118)). The
difference is of minor importance (61). The use of $V_{\text{max}}$ in the
exponential function allows the constant $K$ to reflect the distensibility of the lung independent of lung size. The constant, the half-inflation pressure, is defined as "the increase in transpulmonary pressure necessary to inflate the lungs half way to the maximum pulmonary volume from any resting level" (131). By replotting pressure-volume curves with $\%TLC$ as the volume axis, the chord compliance (expressed as $\%TLC\cdot kPa^{-1}$) is also a measure of lung elasticity independent of lung size. In this way it is directly proportional to $K$ (34). The coefficient of variation of $K$ is only slightly less than the coefficient of variation of chord compliance expressed as $\%TLC\cdot kPa^{-1}$. As they measure the same change in the elastic properties of the lung (33), the method of replotting pressure-volume curves and measuring chord compliance was chosen in the present study.

The correlation between repeated measures of chord compliance was performed on ten subjects seen one week apart. The results suggest that the methods employed in the present study were reproducible ($r > 0.9$), there was no significant differences between the repeated measurements ($p > 0.05$). Also the use of the balloon technique has recently been evaluated (4). Inspecting the data 'by eye' it was evident that pressure-volume curves were sigmoid and a complete description of the curve would not necessarily have any advantage over a simpler function that accurately described the most easily interpreted part of the curve (4). The small part of the pressure-volume curve above functional residual capacity that was used to calculate its slope has been shown to be a good predictor of the rest of the curve but the exponential analysis has the advantage of using more pressure-volume data in its evaluation. Perhaps the exponential analysis should be used in future studies as the constant $K$ is not markedly affected by differences in measuring techniques. If all studies used the exponential function it would be easier to make comparisons of the results.

The results from the present study were within the ranges reported for young men aged 24-29 years and those given for adult populations (37, 63). The measurements of lung compliance, when reported in the literature, are usually obtained from the
expiratory, deflation pressure-volume curve. The transpulmonary pressure at a given lung volume is greater on the inflation pressure-volume curve due to the different number of contributing units and the surface tension and elastic tissue forces in the alveoli (61). As a result of this hysteresis, the expiratory pressure-volume curve reflects the elastic behaviour of the lung more closely than the inspiratory pressure-volume curve. In a recent study it was suggested that both curves should be obtained as the two are not specifically related and cannot be predicted from each other (113). It has been suggested that the inspiratory pressure-volume curve is more useful in patients with lung disease as it is more easily obtainable and therefore more reproducible (168). In the present study, the data on ten subjects who repeated measurements of lung compliance after a seven day interval demonstrated that the expiratory pressure-volume curves were more reproducible.

6.6 Does the lung expand or grow within the larger thoracic cavity during development?

The two study groups in the cross-sectional study were similar in stature, weight, respiratory muscle strength and all other anthropometric measurements except chest width and sitting height. The difference in lung volumes between the groups was paralleled by the difference in chest widths. This result was expected as the conclusion from the longitudinal study was that chest width contributed to the description of lung volumes during the study period. Although the lung volumes are greater in the group of men with the greater chest widths, the subdivisions of total lung capacity are similar when expressed as a percentage of TLC (RV/TLC%, FRC/TLC%) (Table 5.19). This suggests that the group with the larger chest widths do not simply possess the same size lung, which has expanded within the enlarged thoracic cavity, as the group with the smaller chest widths. It indicates that the lung has actually 'grown' within the larger chest cavity.

This growth may be a combination of the hypertrophic and hyperplastic development of the alveoli which may occur into adulthood (48). The phenomenon of lung growth within an
'enlarged' thoracic cavity has been demonstrated in animal studies where compensatory growth depends on the age at which the pneumonectomy is carried out (103, 124). If the lung is developing by multiplication of alveoli (cellular hyperplasia) then the compensatory growth is by multiplication of units. If the lung is growing by increasing the cell size (alveolar hypertrophy) growth is by expansion of units. The latter gives a smaller increase in lung size in animal studies (85). The fact that lung growth within an enlarged thoracic cavity may occur at any age is shown by the general visceromegaly of acromegaly in humans (19). This results from actual lung growth; it has been suggested that this is due to an increase in the size rather than the number of alveoli. In the present study, the mechanism by which the lung grows to increase its volume is speculative.

6.7 Does the lung increase in size as a result of changes in the elastic properties of the respiratory system?

The longitudinal study demonstrated that between the ages 18-19 years there was an increase in lung volumes which was associated with an increase in the thoracic dimensions, particularly chest width. Changes in the elastic properties of the respiratory system may have accounted for the increase in thoracic dimensions by altering the position of the thoracic wall. This has already been suggested in relation to the changes in the subdivisions of lung volume (Section 6.2). If this had occurred, the two groups with different lung volumes in the cross-sectional study would have had significantly different elastic forces at given lung volumes. However, the results indicate that the recoil pressures at TLC and TLC-20% VC were similar (Table 5.21).

The two sample groups in the cross-sectional study were shown to have different values for chest width which was expected from the longitudinal study results. The reason for this difference in chest widths may be either growth of the thorax or an increase in the outward recoil of the chest wall. The outward recoil of the chest wall is balanced by the inward recoil of the lung at functional residual capacity (the 'resting' position of the thorax). The two study groups had similar lung recoil pressures at FRC ($E_{FRC}$; $I_{FRC}$) which suggests that the outward recoil of the
chest wall at FRC was also similar. It is most likely that the
difference in chest widths between the groups was due to growth
of the thoracic cage rather than a change in the outward recoil
of the chest wall. This implies that the increase in the size of
the lung is not due to changes in the elastic properties of the
respiratory system.

6.8 Is there an association between the size of the trachea and
the size of the lung?

The tracheal dimensions and cross-sectional area were not
correlated with the size of the lungs (Table 5.23). This finding
was in agreement with others (35, 51, 84, 90), although using the
technique of acoustic reflection a weak association between them
has been reported (22). The lack of correlation between airway
and lung size supports the theory of dysanaptic or non-isotropic
growth. This theory proposes that the reason for individuals
with the same lung size and lung recoil having different maximal
flow-volume curves is due to the variation in airway size (68).
If dysanaptic growth occurs the airways and lung parenchyma
develop at different rates so there is no relationship between
airway size and lung volume. Mead demonstrated this using flows
to signify airway size (105) but this has been confirmed in later
studies where direct measurements of tracheal size were obtained
(35, 84). The present study also finds no correlation between
tracheal size and lung volume.

The men with the larger thoracic volumes were found to have more
distensible lung tissue. This may offer some advantage which
would be emphasised at the apex of the lung where the pleural
pressure is more negative due to the gravitational gradient. The
pressure difference is about 0.019kPa for every 1cm distance down
the lung (61). The extra-pulmonary trachea is influenced by the
local pleural pressure in the apex of the thorax without being
affected by the pulmonary compliance. The tracheal dimension and
tracheal cross-sectional area measured at total lung capacity
were similar in the two cross-sectional study groups. This
suggests that the pleural pressure within the apex of the thorax
at TLC was the same in both groups and may allow the more
distensible lung tissue to expand to a greater extent at TLC.
This may have important implications and contribute to the differences at large lung volumes between the groups.

There are several methods used to measure tracheal dimensions which make it difficult to compare the results reported in the literature. Most investigators who have used radiographic techniques have failed to use or report the magnification correction factors which are necessary to validate the results. The more recently reported methods of acoustic reflection and computed tomographic scanning (CT scanning) may be more accurate and more acceptable to the subject. However, in large epidemiological surveys these methods are expensive and impracticable. The results in the present study were obtained from tracheal segments on chest X-rays (60, 116). In men aged 19 years the values were consistently lower than others in the literature for adult populations (see below). The difference may be due to the men being younger in the present study than in other study populations, as the trachea increases in size with age (60).

<table>
<thead>
<tr>
<th>Author (Ref)</th>
<th>Age (Mean)</th>
<th>XTRAC (cm²) Mean (SD)</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knudson 1983 (90)</td>
<td>69.3 yr</td>
<td>2.2 (0.48)</td>
<td>X-ray</td>
</tr>
<tr>
<td>Dolyniuk 1986 (51)</td>
<td>4-20 yr</td>
<td>3.5 (0.57)</td>
<td>CT scanning</td>
</tr>
<tr>
<td>Breatnach 1984 (18)</td>
<td>27.9 yr</td>
<td>3.0 (0.70)</td>
<td>X-ray</td>
</tr>
<tr>
<td>Hoffstein 1986 (84)</td>
<td>32 yr</td>
<td>3.6 (0.53)</td>
<td>X-ray</td>
</tr>
<tr>
<td>Collins 1986 (35)</td>
<td>50 yr</td>
<td>3.3 (0.73)</td>
<td>Acoustic reflection</td>
</tr>
<tr>
<td>Gibellino 1985 (60)</td>
<td>21.1 yr</td>
<td>2.81 (0.38)</td>
<td>X-ray</td>
</tr>
<tr>
<td>Osmanlieu 1982 (116)</td>
<td>20.6 yr</td>
<td>3.1 (0.40)</td>
<td>X-ray</td>
</tr>
<tr>
<td>Present Study</td>
<td>19 yr</td>
<td>2.0 (0.31)</td>
<td>X-ray</td>
</tr>
</tbody>
</table>

The longitudinal study results have already shown that the 19 year old men in the present study are a 'growing' population. The tracheal dimensions were similar to the results in a study of
a population less than 20 years old (69) but it is difficult to compare the results as the mean age was not reported in the latter study.

Most tracheal dimensions are reported at total lung capacity as the sagittal section is clearer at TLC than at RV (116). It has been reported that the tracheal dimensions at TLC are similar to those at RV (116). Others have found that they are greater at TLC using acoustic reflection and CT scanning techniques (52, 84). The present study used chest X-rays at TLC as a standard to compare the two study groups at full lung volume.

6.9 Do differences in physical activity and muscular strength contribute to the differences in lung growth between individuals?

It was evident that the two study groups in the cross-sectional study had similar profiles for levels of physical activity (Table 5.16). Although the numbers of subjects in each group were small, it must be concluded that the differences in lung growth were not associated with muscular development or physical activity. However, the present study did not include objective measurements of physical fitness that may have indicated an association with lung growth. A criticism of the present data is that they are restricted to subjective reports of physical activity and more objective data on physical fitness would be necessary to ensure firmer conclusions.

There has been recent interest in this subject as sporting activity is related to lung function and, although it has been shown to contribute little to the prediction of lung function when height and age are included (27), there is a correlation between the level of fitness and lung function independent of smoking status (139). The increase in lung function associated with physical exercise has recently been reported in a study involving young swimmers 17-21 years old (31). By training the inspiratory muscles a group of swimmers increased their vital capacity and functional residual capacity over the training period. This suggests that changes in lung volume may occur due to the level of physical exercise but the group of swimmers

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performed specific endurance training to produce this result. The authors remarked that normal lung growth in this age group may have contributed to the change in lung volume and the present study data has shown that lung growth is evident in the 17-19 year old men. Because the two sample groups in the present cross-sectional study had similar profiles of reported sporting activity and were not in 'special' training it may be that the difference in lung volumes between them was not associated with their levels of physical activity.

Respiratory muscle strength was reflected in the measurement of maximal respiratory pressures (MIP, MEP, kPa). In the longitudinal study the maximal inspiratory pressures increased between the ages 18-19 years; this was accompanied by a decrease in the maximal expiratory pressures. The change in the resting position of the lung and chest wall at functional residual capacity may facilitate an increase in the inspiratory pressure whilst limiting the expiratory pressure. There was no evidence that the increase in lung volumes was associated with the change in the respiratory muscular strength (Table 5.9). In the cross-sectional study, the two groups with different lung sizes had similar maximal respiratory pressures (Table 5.2). This also indicated that the respiratory muscular strength is not associated with or a consequence of lung growth in the study population. It may be that in this age group 17-19 years other factors, such as the change in the thoracic dimension, are more important in contributing to lung growth.

The measurements of maximal respiratory pressures have been widely reported in the literature. Although technical differences are evident between studies, most report maximal inspiratory pressure at RV and maximal expiratory pressure at TLC. The within-subject coefficient of variation is less than 10% and the group coefficient of variation is less than 25% (10, 159, 166). There are several ways to reduce the variability of these measurements which have been outlined recently (142). The most relevant of these with regard to the present study is the number of trials necessary to produce the highest mouth pressure. There is a learning effect associated with the measurement which has led to the recommendation that as many as 20 trials are
recorded (159); however once the subjects become familiar with the procedure their achieved pressures do not improve. Recently, Szienberg has recommended the recording of 5 or more trials as lower values are reported in studies using only two or three trials (146). In the present study the manoeuvre was repeated until two satisfactory consecutive results were obtained. This was in accordance with the original study introducing maximal respiratory pressure measurements (10).

Another difference between the reported methods for measuring maximal respiratory pressures that may influence the results of the present study is the use of a rigid cylindrical mouthpiece. Studies which have consistently underestimated the mouth pressure have used a scuba-type mouthpiece (146). This flexible, rubber mouthpiece may influence the result by altering its dimensions under pressure. The rigid, cylindrical mouthpiece maintains its shape; in the present study it was clenched by the teeth and the lips were supported by a ridge to prevent air leaking around the mouth.

The reference values for maximal respiratory pressures are usually reported for populations spanning the entire age range from childhood to adulthood. Few studies give values that are specific to the age group 17-19 years; Wilson reports values for children and adults separately, the groups are separated at 18 years of age (166). Maximal inspiratory pressures are reported to be lower than maximal expiratory pressures (98, 142, 146, 159). The results in the present study are comparable to those in the literature (142, 166). The results are influenced by the strength of the respiratory muscles which can be improved by athletic training (31). Lung mechanics, particularly of the chest wall, may also influence the respiratory pressures measurement.

6.10 Implications and Future Considerations

The implications of the research presented in this thesis necessarily involve several fields of study including: human biology, physiology and applied medicine. Such research should
In human biology, the interest lies in the use of these data to describe the changes occurring in the population between the ages 17-19 years. It has been stated that the results will strictly only apply to those in heavy industry but the implications may extend to this age group in the general population. The suggestion that lung growth 'overtakes' the growth in stature, in direct contrast to the processes occurring at puberty, is important when fitting growth models to lung volume data. Future work in this field should involve more detailed analysis of longitudinal data. The data should be extended to a greater age range, perhaps 10-20 years old, to give a model of lung growth. Ideally the measurements should be obtained at six-monthly intervals to monitor the changes more closely and deduce the timing of events more accurately.

In human physiology, the data presented in this thesis lead to speculation of the mechanisms involved. The changes in lung volumes, elasticity and the underlying process of tissue growth combine to describe a complex picture of lung development. These findings could be further investigated by introducing lung compliance measurements into longitudinal studies in future. Longitudinal data are preferable but are more difficult to obtain due to the cost of longitudinal surveys and the difficulties in measuring populations over a lengthy time interval. The use of exercise studies to obtain objective levels of physical fitness has already been mentioned in order to investigate the differences in physical activity between individuals.

In the field of applied medicine, the present data have implications on the use of reference values. Thoracic dimensions should be included in such equations as the increase in chest width has been shown to influence the increase in lung size. However, more data is required to provide more accurate prediction equations and future studies should include thoracic dimensions as routine measurements.
There is currently much interest in the effect of smoking on lung function in young populations. The implications of initiating the smoking habit and the prediction of adult lung function based on measurements taken in the age group 17-19 years have important considerations in clinical medicine. The present study was not designed particularly to analyse smoking habits but the two study groups, in the cross-sectional study, those with large TLC values (n=27) and those with small TLC values (n=27), were shown to have similar numbers of smokers and non-smokers. In this respect the sample groups were comparable but smoking has an effect on lung function even in this young age group (7). It has been reported that in young populations, where the smoking habit has been initiated or has only just recently begun, young male smokers have greater lung function than those who have not taken up the habit (27). This has been explained as being due to:

i) the stimulative effect of inhaled nicotine on the local lung tissue;

ii) compensatory growth of the lung caused by inhaled carbon monoxide;

iii) loss of lung elastic recoil as a result of inhaled irritants (96).

An alternative suggestion is that young people with respiratory symptoms (114) or poor lung function (152) are less likely to initiate the habit. In the present study the two sample groups had similar profiles of respiratory symptoms (Table 5.17). However, those who reported a history of asthma were excluded from the longitudinal survey population and, therefore, not included in the cross-sectional study. A history of asthma has an adverse effect on lung volumes (58, 126).

There is a "cross-over effect" where the lung function of smokers deteriorates below the level of non-smokers (152). This probably occurs later than 19 years of age, the end point in the present study, as the decline in lung function with smoking is related to the duration of the habit and the number of cigarettes smoked per day (7).

It is unlikely that smoking can account for the differences in lung volume between the sample groups; (there were 27 subjects in
each group and the majority of men were non-smokers (19 and 17 men respectively)). Future studies are needed which are designed specifically to investigate the initiation and possible cessation of smoking with respect to lung growth in this age group.
CHAPTER 7

CONCLUSIONS
i) The rate of lung growth exceeds that of stature just prior to the cessation of somatic growth.

ii) The subdivisions of lung volume grow at different rates; the functional residual capacity contributing more to the increase in total lung capacity during the ages 17-19 years.

iii) The increase in lung size is attributed to an increase in the thoracic dimensions; the chest width increasing more than chest depth.

iv) The increase in chest volume is not due to lowering of the diaphragm.

v) The development of the lung is associated with the distensibility of the lung tissue; those with large lungs have less elastic recoil.

vi) The lung develops within an enlarged thoracic cavity due to tissue growth.

vii) Increase in lung size is not due to changes in the elasticity of the respiratory system.

viii) There is no correlation between the size of the trachea and the size of the lung; this is in agreement with the concept of dysanaptic growth.

ix) The level of habitual exercise and muscular strength are not the major factors contributing to lung growth during the 17-19 year old age group.


APPENDICES
APPENDIX 1

Measurement of Lung Volumes

The Resparameter Mk IV (P.K. Morgan Limited), a water-bell spirometer system, was in closed circuit mode for this procedure. It contained a soda-lime canister to absorb the carbon dioxide produced during rebreathing. Prior to the subject being connected to the Resparameter the gases in the circuit of the apparatus were "flushed out" by opening the inlets and gently raising and lowering the bell. The Resparameter's internal pump was switched on for this but then switched off when the circuit had been "flushed" successfully. The bell was lowered completely and the paper trace was marked with the bell in this position. Approximately 2.5 litres of air were drawn into the system by raising the 9-litre capacity bell. The circuit was closed and the paper trace marked as before. Then 800ml of 100% helium gas and 200ml of 100% oxygen gas were introduced into the system via the 'oxygen in' inlet on the Resparameter. The oxygen compensator on the helium analyser was checked to be reading 21% and the Resparameter's internal pump switched on. When the gases in the closed circuit had mixed thoroughly, the helium reading on the helium analyser remained constant and the initial helium reading was recorded as Helium 1. The paper trace was marked to notify the volume of the closed circuit. The temperature of the apparatus was noted.

The subject, with a tight-fitting noseclip, was seated at a comfortable height for the mouthpiece of the Resparameter. He was connected to the mouthpiece and was asked to breathe quietly for several minutes. During this time he was breathing air to settle his breathing pattern before the test procedure began. It was found that this relaxation was assisted by the subject keeping his eyelids closed. At the end of a tidal expiration (at FRC) the subject was connected to the closed-circuit system. The kymograph was set to a slow paper speed (5cm.min\(^{-1}\)) for the duration of the test procedure. Immediately the subject was connected an oxygen flow of 200-300 ml.min\(^{-1}\) was introduced into the system via the 'oxygen in' inlet of the Resparameter. This was to compensate for the uptake of oxygen and the absorption of carbon dioxide during rebreathing. The oxygen
flow was adjusted periodically to ensure the volume of the system remained relatively constant throughout. The subject continued to breathe normally as the helium readings on the helium analyser were recorded every 30 seconds. These readings fell steadily as the helium in the system was diluted by the lung volume gases which had been introduced into the closed circuit. When the reading remained constant for a period of 30 seconds (within 0.01%) the final value of helium was recorded as 'Helium 2'. The difference between 'Helium 1' and 'Helium 2' is a function of the volume ratio between the lung and the closed-circuit system.

The subject was then asked to expire as much volume from their lungs as possible. They were continually encouraged by the observer. The subject returned to normal breathing and 5-6 breaths were usually necessary to return the trace to 'baseline' tidal volume recording. The subject then repeated the expiratory manoeuvre followed immediately by a full unhurried inspiration to total lung capacity (TLC). When this was completed the subject was asked to return to normal, quiet breathing and allowed to 'settle' again for several breaths. The last two respiratory efforts involved the subject inspiring fully to TLC and then immediately expiring, again unhurriedly, to residual volume (RV). The observer continually encouraged the subject to achieve the maximal effort on all manoeuvres.
APPENDIX 2

Calibration of The Resparameter Mk IV

Checking that the System is "Leak-free"

Always as a twice-daily routine, and whenever the system was inspected or altered in any way, the closed circuit was checked to be leak free. The bell was raised and the circuit completely closed at all apertures. A 2kg weight was gently lowered onto the bell and the Resparameter internal pump switched on. If there was no noticeable decrease in the closed-circuit volume after a period of 20 minutes, the recording on the paper trace remained constant. If any leaks were detected, the apparatus was inspected and the procedure repeated until satisfactory.

Calculating the Dead Space of the Resparameter Mk IV

This was calculated daily and whenever the soda-lime or water level of the Resparameter was altered.

After "flushing out" the apparatus the bell was lowered completely with the Resparameter in the open circuit mode and the pump switched off. The Resparameter was placed in closed circuit mode and the paper trace marked in this position. Then 400ml of 100% helium and 100ml of 100% oxygen were introduced into the system and the Resparameter pump switched on to mix the gases. After a few minutes the pump was switched off and the mouthpiece aperture opened. The bell was gently, but quickly depressed, to its lowest position. The mouthpiece was quickly closed and the paper trace marked in this position. The Resparameter pump was switched on and the initial helium reading (He 1) taken from the helium analyser when a constant value was maintained. The Resparameter pump was then switched off and the mouthpiece aperture opened. The bell was raised quickly to draw in approximately 2 litres of air and the mouthpiece aperture closed again. The paper trace was marked and the Resparameter pump switched on. When the gases were thoroughly mixed the helium level had fallen to a constant level (He 2) and this was recorded. The exact volume of air added to the closed circuit was calculated from the paper trace.
The dead space was then obtained from the following relationship.

\[
\text{Dead space (l)} = \frac{\text{Volume Added (l) \times He } 2 \text{(\%)} }{\text{He } 1(\%) - \text{He } 2(\%)}
\]
APPENDIX 3

Body Markings

Each subject had the following marks made on his body with a dermographic pencil (162). This allowed some of the anthropometric measurements to be obtained more easily and accurately.

a. **Suprasternal Notch**

   The deepest point in the hollow of the suprasternal notch representing the superior border of the sternum.

b. **Medial aspect of the clavicle**

c. **Acromium**

   The inferior edge of the most external border of the acromium process of the scapular bones.

d. **Olecranon Process**

   The tip of the olecranon process of the ulnar bone located when there is flexion at the elbow.

e. **Most lateral aspect of the clavicle**

   Where it articulates with the scapula.

f. **Inferior aspect of the xiphoid process**

g. **Mid-clavicular point**

   Measured by measuring tape as the bisector of line (b) - (e)

h. **Horizontal mark on left upper arm**

   Measured by measuring tape as the bisector of line (c) - (d) when there is flexion at the elbow.

i. **Costal margins**

   Most inferior edge of the fused costal cartilages of false ribs in the mid-clavicular line.
Measurement of Static Compliance

The standard procedure has been described by Gibson and Pride (61); the apparatus is illustrated in Fig 4.3. The spirometer was calibrated using a 3 litre syringe and the transducer/plotter system was calibrated using a water manometer on the day of testing.

The subject was seated at the correct height for the mouthpiece of the compliance apparatus. The head was tilted forward and a straw placed to one side of the mouth through which water could be drawn from a cup. The oesophageal balloon was introduced into the subject's nostril by the observer as the subject was instructed to sip water from the cup and keep his eyes closed. When the oesophageal balloon gave a positive deflection on the differential transducer it was withdrawn approximately 10cm to lie in the lower third of the oesophagus. The placement was adjusted until the greatest negative pressure was obtained when the subject sniffed and the cardiac artefacts were minimal. The subject was then given a noseclip in order to keep the oesophageal balloon in position throughout the test.

The bellows of the spirometer were emptied and the three-way-tap operated so that the mouthpiece was connected to the air. A zero pressure-volume mark was placed on the recording paper trace prior to the test manoeuvre.

Expiratory Lung Compliance

The subject was connected to the mouthpiece breathing air and asked to breathe gently for a few minutes to relax. Three full inspiration manoeuvres were performed with the observer encouraging maximal efforts each time to ensure a constant volume history. On the third occasion when the subject was at TLC the three-way-tap was turned to connect the subject with the spirometer system. The shutter mechanism was started at this point and the pen of the x-y recorder set to paper. The subject was asked to breathe out very slowly as the shutter interrupted the expiration at one second intervals for a period of one second. When the shutter was in operation the flow was

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interrupted and a horizontal excursion recorded on the curve. The pressure at this volume point was measured as the bisector of this horizontal line. When the subject had completed this manoeuvre the three-way-tap was turned again to disconnect the subject from the system. The subject was disconnected from the mouthpiece and the bellows of the spirometer reset for another test. This procedure was repeated until at least two satisfactory expiratory pressure-volume curves were obtained.

**Inspiratory Lung Compliance**

The bellows of the spirometer were inflated with approximately 1 litre of air using the three-way tap system. A zero pressure-volume mark was then established on the paper trace and the subject connected to the mouthpiece. After a full inspiration the three-way tap was turned and the subject connected to the spirometer. He was asked to expire fully into the apparatus while the pen of the plotter was set to paper. The observer encouraged maximal effort from the subject throughout the test. At residual volume the subject was asked to breathe in slowly without 'gulping' as the shutter mechanism operated. At least five shutter interruptions were obtained during inspiration. At TLC the observer encouraged the subject to hold this position for 2-3 seconds as the shutter system continued to operate. The pen was then lifted from the paper trace and the subject disconnected from the mouthpiece. This procedure was repeated until at least two inspiratory pressure-volume curves were obtained.

**Measuring the Pressure-volume Curves**

The curves are sigmoid-shaped and have a linear portion (11), the gradient of which can be calculated from a line fitted by eye to the pressure-volume points. Each curve had to have at least three pressure-volume points, within the linear portion of the curve, from which to determine the line. The inspiratory and expiratory lung compliance (C\text{INS} and C\text{EXP} respectively) were calculated as the mean gradient from at least two satisfactory curves. The expiratory lung compliance was obtained from the expiratory pressure-volume curves and the inspiratory lung compliance was obtained from the inspiratory pressure-volume curves. Both measurements were expressed as a change in volume for a given change in pressure (l.kPa\(^{-1}\)). The maximal
recoil pressure of the lung (RP; kPa) was taken from the inspiratory pressure-volume curves at TLC when the shutter was closed. The pressure was taken as the maximum observed from the satisfactory pressure-volume curves.

The elastic recoil pressure of the lung measured at the lung volume TLC-20%VC (P_{STAT}; kPa) was taken from the expiratory pressure-volume curves. If no shutter operated at this precise volume, the pressure was measured at the exact point on the curve where this volume of the lung occurred. The mean value from at least two satisfactory expiratory pressure-volume curves was accepted as the recoil pressure at TLC-20%VC for each subject. The vital capacity was taken as the expiratory vital capacity from the spirometer trace obtained on the same day of testing.
APPENDIX 5

Chest X-ray Magnification Factors

Enlargements = F.F.D. (Focus to film distance)
Magnification = F.O.D. (Focus to object distance)

Where:-

F.F.D. = 183cm

To find F.O.D. using the metal coin markers:-

Actual size = Recorded size x F.O.D.  

\[
F.O.D. = \frac{(Actual\ Size) \times 183cm}{(Recorded\ Size)}
\]

Posterio-Anterior X-rays to determine P.T.D.

Left hand side coin (positioned on front of chest)

F.O.D. = \( \frac{(2.8)(183)}{3.3} \) = 155cm from focus

Right hand side coin (positioned on back of chest)

F.O.D. = \( \frac{(2.8)(183)}{2.87} \) = 178.5cm from focus

Distance of trachea from focus = \( \frac{(178.5 - 155) + 155}{2} \)

= 166.8cm
Posterio-anterior X-rays

Magnification = F.F.D. = \( \frac{183}{166.8} = 1.097 \)

Since:

\[
\text{Actual Size} = \text{Recorded size} \times \frac{\text{F.O.D.}}{\text{F.F.D.}}
\]

Tracheal Diameter (PTD) cm = Measured Diameter \( \times 0.9116 \)

Lateral Chest X-rays to determine L.T.D.

F.O.D. = \( \frac{(2.8)(183)}{3.25} = 157.7 \) cm

Magnification factor = \( \frac{183}{157.7} = 1.160 \)

Since:

\[
\text{Actual size} = \text{Recorded size} \times \frac{\text{F.O.D.}}{\text{F.F.D.}}
\]

Tracheal Diameter (LTD) cm = Measured Diameter \( \times 0.862 \)
APPENDIX 6

Reproducibility of The Methods

Pressure - Volume, Curve Measurements

Ten subjects performed inspiratory and expiratory pressure-volume curves at the same time of day and on the same day of the week on two occasions ($x_1$, $x_2$). The occasions were separated by an interval of seven days. The methods of obtaining lung compliance ($C_{INS}$, $C_{EXP}$) and elastic recoil ($RP$, $P_{STAT}$) were as described previously and used in the present study.

The results were analysed using correlation coefficient ($r$), paired Student's t-test ($p < 0.05$) and mean percentage changes ($\Delta x/\bar{x}$ %) (115).

<table>
<thead>
<tr>
<th></th>
<th>$x_1$</th>
<th>$x_2$</th>
<th>$r$</th>
<th>t-value</th>
<th>% change (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{INS}$ (1.kPa$^{-1}$)</td>
<td>2.51</td>
<td>2.37</td>
<td>0.94</td>
<td>1.96 NS</td>
<td>7.9</td>
</tr>
<tr>
<td>$C_{EXP}$ (1.kPa$^{-1}$)</td>
<td>3.14</td>
<td>3.18</td>
<td>0.98</td>
<td>0.62 NS</td>
<td>6.6</td>
</tr>
<tr>
<td>$RP$ (kPa)</td>
<td>3.08</td>
<td>2.99</td>
<td>0.92</td>
<td>0.87 NS</td>
<td>8.1</td>
</tr>
<tr>
<td>$P_{STAT}$ (kPa)</td>
<td>1.05</td>
<td>1.09</td>
<td>0.72</td>
<td>0.60 NS</td>
<td>1.57</td>
</tr>
</tbody>
</table>

NS - not significant
Anthropometric Thoracic Dimension Measurements

Eleven subjects had thoracic dimensions measured on two occasions \((x_1, x_2)\). The occasions were at least seven days apart and the methods used have been described previously.

The results were analysed using correlation coefficient \((r)\), paired Student's t-test \((p < 0.05)\) and the mean difference calculated in millimetres \((\text{mm})\).

<table>
<thead>
<tr>
<th>Dimension</th>
<th>(x_1)</th>
<th>(x_2)</th>
<th>(r)</th>
<th>Mean Difference (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STERNL(mm)</td>
<td>206</td>
<td>208</td>
<td>0.66</td>
<td>2.36</td>
</tr>
<tr>
<td>LCML(mm)</td>
<td>317</td>
<td>316</td>
<td>0.93</td>
<td>1.45</td>
</tr>
<tr>
<td>RCML(mm)</td>
<td>317</td>
<td>316</td>
<td>0.92</td>
<td>1.18</td>
</tr>
<tr>
<td>CHW(mm)</td>
<td>278</td>
<td>274</td>
<td>0.75</td>
<td>3.45</td>
</tr>
<tr>
<td>CHD(mm)</td>
<td>191</td>
<td>187</td>
<td>0.92*</td>
<td>4.00</td>
</tr>
</tbody>
</table>

* Significant \((p < 0.05)\)