PATHOLOGY OF CHRONIC BRONCHITIS AND EMPHYSEMA

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TO MY WIFE JOAN

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Preface

Some of the most notable advances in medicine since the war have been concerned with respiratory diseases. The greatest has been the control of tuberculosis, but almost as remarkable have been advances in knowledge of chronic bronchitis and emphysema, the approach to which has been exceedingly wide with planned collaboration between workers on all aspects of the problems. Both practical and fundamental issues have been reanalysed and developed, and pulmonary pathology has contributed usefully to these studies. Examples of this collaborative approach may be read in the reports of the outstanding Annual Conferences on Research in Emphysema at Aspen, Colorado (1958–1968), of the Ciba Foundation Symposia in London (1959, 1962), the recent meeting in Birmingham, England (1968) and the book entitled 'The Lung' edited by Liebow and Smith (1968). For the pathologist, this is a stimulating circumstance since he can plan his work with the composite picture in mind, and can be happy that the functional implications of his structural findings will be appreciated by a wide audience.

The intentions of this new book are to describe and illustrate the structural changes which may be present in the lungs of patients with chronic bronchitis and emphysema, to review recent research on these subjects and to consider the functional implications of the structural findings. It is based on pathological investigations carried out over the last 14 years in the Royal Postgraduate Medical School of London and in the University of Edinburgh. Pathological anatomy and histology remain as an essential foundation of knowledge about disease, without which basis the concepts of many diseases are easily distorted (Anderson, W.A.D., 1948). This is especially the case with emphysema where speculation without regard to structural changes has led to a great deal of confusion over the years and to a multiplicity of terms—I have collected 148 in English alone. In the following account, only widely-accepted terms relating to structure are employed, and the number has been reduced to a minimum by discarding, after brief mention, those terms which imply mechanisms that may turn out in time to be incorrect or of minor importance, and also many terms which are synonymous.

The classification of emphysema proposed is based on changes in the pulmonary lobule and is arranged to include classical and current views. The lobule has been selected as the basis in preference to the acinus because it appears to be the most widely-used unit of reference at the present time. The names panlobular and centrilobular emphysema are chosen on this account. It is important to appreciate, however, that since the acinus is considered by some to be a better defined structure anatomically than the

lobule the names panacinar emphysema (Ciba Guest Symposium, 1959) and centriacinar emphysema (Reid, 1967) are favoured. Provided, however, that the reader is aware that the two sets of terms refer to the same pathological conditions, and accepts them interchangeably in different accounts, no confusion should result.

Methods are important in studying lung structure and newer findings have depended on them. For this reason they are dealt with at some length in the text and partly from an historical point of view. Many workers use paper-mounted whole lung sections (Gough and Wentworth, 1949, 1960) and prefer them to whole lung slices on account of their convenience in handling. The appearances described and illustrated in this book relate to slices rather than sections, but the accounts should be found useful in reading whole-lung sections. Slices are easy and quick to prepare and reveal a great deal of information due to their three-dimensional structure. Barium sulphate impregnation is used to improve the visibility of alveolar walls when the slices are viewed in water.

For functional and clinical approaches to chronic bronchitis and emphysema the reader is referred to the works of Stuart-Harris and Hanley (1957), Oswald (1958), Campbell (1958), Cherniack and Cherniack (1961), Comroe and co-workers (1962), Cunningham and Lloyd (1963), Bates and Christie (1964), Cotes (1965), West (1965) and Filley (1967).

I am greatly indebted to a number of persons for help in this work, but especially to my wife, Mrs. Joan Margaret Heard, who has spent so much time typing the script and helping with the references. I am also indebted to Mr. W. H. Brackenbury, Mr. J. Paul and Mr. T. C. Dodds for the photographs, to Professors C. V. Harrison and G. L. Montgomery for their interest and advice, to Dr. C. M. Fletcher, Dr. T. Simpson and Dr. J. W. Laws for clinical and radiological co-operation, and to Professor G. Restrepo, Dr. T. Izukawa, Dr. J. Esterly, Dr. A. Reid, Dr. J. Wootliff, Dr. L. Macleod and Dr. S. Hossain for help with the pathological investigations.

For permission to reproduce from my published papers, I am indebted to the Editor of *Thorax* for Figs. 3.1, 3.4, 3.5, 3.6, 6.2, 6.4, 6.6, 6.7, 6.9, 7.11, 7.15, 8.1 and 10.1 etc., the Editor of the *American Review of Respiratory Diseases* for Figs. 2.1, 7.10, 9.3 etc., the Editor of *Medicina Thoracalis* for Figs. 3.5, 3.6, 6.4 etc., the Editor of the *British Journal of Radiology* for Figs. 9.5, 14.1, 14.2, 14.3 and 14.4 etc., the Editor of the *Journal of Pathology and Bacteriology* for Figs. 3.2, 3.3, 6.3 and 7.1 etc., Niederrheinische Druckerei GmbH, Dinslaken, for Fig. 7.1, Longmans, Green and Co. Ltd. for Figs. 7.3, 7.8, 7.14 and 9.4, and Pergamon Press for Fig. 7.4.

The author wishes to thank the publishers, J. and A. Churchill Ltd., for their consideration and courtesy. It is an especial pleasure to recall that John Churchill, London, published the monograph on emphysema by A. H. T. Waters in 1862.

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Contents

PART 1. EMPHYSEMA

I A Brief Historical Review of Methods Employed for Emphysema

Early descriptions of emphysematous lungs were made long before formaldehyde was introduced as a fixative by Blum in 1893 and also before the optical microscope became available. Lungs were dissected in the fresh state and air spaces and interspaces were distended with air by blowing through a pipe (Watson, 1764; Baillie, in several editions of a book from 1793 to 1833). The course of bronchi and blood vessels was traced by the injection of coloured liquids (Willis, 1676) or mercury (Malpighi, 1697; Reisseisen, 1808). Details of the early methods may be obtained from reviews by Kountz and Alexander (1934), Miller (1937) and Strawbridge (1960a). The most important early work was by Laennec (1819, 1821, 1846), who inflated lungs with air and dried them. It was on such specimens that he described how 'vesicular or pulmonary emphysema, properly so-called', appeared to be 'mere dilatation of the vesicles of which the viscus is composed', although intermediate partitions were often ruptured. In a monograph on emphysema written just over a century ago, Waters (1862) described lobules and lobulettes in air-dried lung, the former being probably the same as the modern lobule (secondary lobule of Miller), and the latter the modern acinus. His subdivisions of the patterns of emphysema are still of great value today (page 24).

With the development of the optical microscope, Rainey (1848) described how the pulmonary membrane lining the air cells appeared perforated and cribriform in emphysema, the holes being of various sizes and oval or circular in outline. He worked at a magnification of 'twenty or thirty diameters'. Thin slices of dried lung were used for microscopy by Schultz (1850) and Schulze (1871). Mandl (1857) injected normal lungs with gelatin, allowed them to dry, cut thin slices, moistened them with water and examined them under the microscope. Rindfleisch (1872, 1878), Nicolas (1898) and Loeschke (1921) used corrosion preparations, but Miller (1937) considered they were 'practically useless' for studying the minute structure of the lung, and thought no method of investigating the lung gave 'so varied and erroneous an idea of its structure'. Eppinger (1876) and Orsós (1907) and Loeschke (1921, 1928) studied the elastic tissue and collagen of the lung in emphysema microscopically, and Kohn (1893) described the alveolar pores in normal lungs.

METHODS USED IN RECENT YEARS

FIXATION

Distension of the lung by an aqueous fixative. Hartroft and Macklin (1943, 1944) distended the lungs with formalin, slowly at first to let the air out, then at 75 cm. water pressure until the length of the lung equalled an intrathoracic measurement. The lung was floated on 3 per cent formalin and the size checked periodically. Gough and Wentworth (1949, 1959, 1960) distended the lungs fully via the bronchi with a mixture of liq. formaldehyde (40 per cent) 500 ml., sodium acetate 200 gms. and water 500 ml. The lung was placed in a container of fixative, covered with a cloth and fixed for 2 days or longer. These latter workers did not tie the bronchus and a disadvantage of this is that the lung may flatten, and shrink unevenly in consequence, by even one-third or more of its volume. McLean (1956a) used a similar method.

In 1958 I introduced continuous pressure fixation with fluid to overcome the flattening and shrinkage (Heard, 1958). A pressure of 25–30 cm. of aqueous formalin via the bronchi was maintained for 72 hours (page 7). A report of the Committee on Preparation of Human Lungs for Macroscopic and Microscopic Study (1959) in the United States recommended distension at that pressure, but afterwards only tying the trachea. Wright (1961) distended the lungs with Zenker's solution via the bronchi for 2 hours partly immersed in fixative, followed by compressed moist air at a pressure of 20 cm. of water for 12 hours. Trapp and Allen (1963) distended the lungs with aqueous formalin at a constant pressure of 90 cm. of formalin for 48 hours. Kleinerman and Cowdrey (1964b) distended the lungs with neutral buffered formalin via the bronchi and continued for 10 to 14 days at a pressure of 2 to 5 cm. of formalin in the vertically supported bronchus.

Suction applied to lung. Continuous suction was applied to a lung suspended in a container by Moolten (1935), who put first coal-gas (to redden haemoglobin) then a fixing solution (Kaiserling I) into the bronchus. A disadvantage of this method is that the lung undergoes some distortion as it hangs by the hilum. Hartung (1957, 1960) applied suction to a lung, and drew formalin into the cannulated bronchus. He related the volume to formulae for normal volumes or the individual's clinical measurements. Formalin cannot be recirculated easily when suction is used.

Perfusion of vessels with fixative. Loeschke (1928) and McLean (1956a) fixed some of their lungs with intravenous formalin via the femoral vein, the femoral artery being opened. A disadvantage of this method is that it perpetuates collapse of the bases of the lungs dating either from the terminal hours of life as in coma, or occurring after death. Carter and Marsden (1956) also used this method to fix experimental animals with pulmonary anthrax. Incidentally, they used air flowing through a jet to transport fluid to a reservoir. Recently we have perfused the pulmonary arteries in addition to the bronchi during pressure fixation, at the same time ligating the pulmonary veins.

Distension with air and drying. This method was employed by the early workers Malpighi (1697), Laennec (1819, 1821, 1846), Rossignol (1846), Schultz (1850) and Schulze (1871), Waters (1862) and others (see page 1). Oderr (1957) and Oderr and co-workers (1958,

1959) injected 500 ml. of 95 per cent alcohol into bronchi before drying with air at 25–30 cm. of water for 4 to 5 days. The disadvantages of air-drying are distortion by shrinkage, and the unsuitability of the tissue for subsequent histology.

Formalin fumes and drying. Blumenthal and Boren (1959) bubbled air through 40 per cent formalin at room temperature for 3–5 days, and air alone for 7 further days. Pratt and Klugh (1961) caused lungs to 'breathe' fumes from formaldehyde at 60°C for 12 to 18 hours by means of a piston. This was followed by drying for 5 to 8 days. Hentel and Longfield (1960) passed air through formaldehyde, a drying agent and 95 per cent alcohol (with a small quantity of acetic acid) before putting it into the lungs for 7 days. Another variation was by Côté *et al.* (1963), who passed air through 10 per cent formaldehyde and into the lungs for 3 days, followed by 95 per cent alcohol for 3 days, absolute alcohol for 2 days and air alone for 5 days. The pressure selected was that which slightly separated the lobes. The above disadvantages of air-drying apply here also.

Formalin fumes (lungs not dried). Weibel and Vidone (1961) applied suction continuously to the lung in a container and introduced the fumes of boiling formalin intrabronchially (2 parts of 40 per cent formaldehyde and 1 part of water). The lung was inflated to just above the point of inflection of the pressure-volume curve. The method is quick, taking only 2–3 hours, but the disadvantages include the additional effect of heat on the lung, which becomes firm and undergoes considerable shrinkage (linear dimensions fall 18 per cent). The shrinkage may well affect different structures in the lungs to differing degrees (Heard and Harding, 1969), although Weibel (1968) does not accept this. Cureton and Trapnell (1961) distended lungs with air bubbled through 40 per cent formaldehyde at room temperature (half empty carboy) at a pressure of 40 mm. of mercury applied continuously. Duguid and Lambert (1964) boiled the formaldehyde for 2 hours, then kept it warm for 5 to 7 days. An air pressure of 10 to 15 cm. of water was applied continuously. Greenberg and co-workers (1964) distended the lungs at three-quarters of maximal specimen inflation, and used fumes from boiling 40 per cent buffered formaldehyde intrabronchially. Silverton (1964) also used formaldehyde fumes and later reviewed this and other methods of fixation (Silverton, 1965).

METHODS AVAILABLE FOLLOWING FIXATION

When a lung has been fixed in the distended position with aqueous fixative, little more is required to identify emphysema than the examination of the cut surface naked-eye in a dish of water, and by means of a dissecting microscope. The treatment of wet slices with barium nitrate followed by sodium sulphate is described on page 9 (Heard, 1958). By improving the contrast of alveolar walls in water, this procedure increases the amount of information obtainable from viewing the cut surface with a dissecting microscope. Photographs may be taken at a higher magnification than previously by Loeschke (1928) and McLean (1956a). The value of coloured injections of vessels for cut surface photographs was shown by Wyatt *et al.* (1962). Direct examination of the cut surface is also rewarding after air-drying and after fume fixation.

Gough and Wentworth (1949, 1960) described a method for embedding whole-lung slices in gelatin, cutting sections 400 μ thick on a large microtome and mounting them on paper. The sections also could be stained and mounted, or examined under water unmounted. As Gough (1967) pointed out, the advantages of the technique are that the preparations can be filed with other papers and are convenient for sending through the mail. It should be appreciated, however, that they give only a two-dimensional view of the lung, and the grain of the paper partly obscures the details of alveoli. For these reasons, and for technical simplicity, I prefer to examine slices 8 mm. thick in water and have devised barium sulphate-impregnation.

Kleinerman and Cowdrey (1964b) stained and mounted 200–500 μ thick sections from blocks of tissue 7 by 5 by 0·5 cm. embedded in gelatin. Various stains were used. This method gives cellular details but cannot be used easily for screening whole-lung slices. Some workers have embedded whole-lung slices or sections in plastic with success.

Air-dried lungs are easily sliced with a sharp knife or meat slicer and examined untreated (Laennec, 1819; Tobin, 1952; Oderr, 1957; Oderr *et al.*, 1959; Blumenthal and Boren, 1959; Pratt and Klugh, 1961; Boren, 1962). Shrinkage, fragility and especially loss of histology are serious disadvantages of this method. Fume-fixed lungs may be cut with a large knife in a similar way; Weibel and Vidone (1961) re-immersed them in Zenker's fluid for 12 hours to stiffen.

Following good fixation, serial sections cut in paraffin wax can be used for three-dimensional reconstructions. Techniques for cine film and serial sections have been described by us and others (see references on page 20).

METHODS FOR PULMONARY ARTERIES AND VEINS

Besides the injection of coloured materials mentioned above (pages 1 and 3), vessels may be studied by the radiography of thin slices of lung (Oderr, 1957; Oderr *et al.*, 1958, 1959). The injection of pulmonary vessels by a radio-opaque mixture (e.g. barium sulphate and gelatin) which sets and remains *in situ* is a valuable aid (Short, 1956). Reid (1967) illustrated the use of this method in emphysema. She employed the following mixture: 500 ml. 'Micropaque' (Damancy & Co.), 50 gms. gelatin powder, 200 ml. water and a few menthol or phenol crystals. Other injection masses are described by Liebow and co-workers (1947), and Carrington (1968).

METHODS FOR PULMONARY CAPILLARIES

Reid and Heard (1962, 1963) injected an India ink-gelatin mixture into pulmonary vessels and examined the capillaries in frozen sections 250 to 500μ thick (Figs. 3.5 and 3.6). With experimental animals, Staub (1961) froze the lungs by pouring on liquid propane cooled with liquid nitrogen to −180°C. Wyatt (1964) injected opaque or coloured latex via arteries or veins; pressures from 100 to 300 mm. of mercury were required.

METHODS FOR ISOLATING ELASTIC AND COLLAGEN

For details of these procedures reference should be madé to the original articles (Lowry *et al.*, 1941; Pierce *et al.*, 1959; Carton *et al.*, 1960, 1964). The other tissues are dissolved away by sodium hydroxide or formic acid, and the elastic etc. remain as a skeleton.

METHODS FOR INTERLOBULAR EMPHYSEMA

With this condition it is necessary to take care not to disturb the air (or gas). Fisher and Macklin (1940) photographed the contents of the thorax, then removed them *en masse*, ran Bouin's fluid 'at low pressure' into the trachea by a tied-in cannula, and clamped the tube. The specimen was immersed in Bouin's fluid. With experimental animals, Ovenfors (1964) dissected out the whole thorax with ribs and spinal column, and made openings in the chest wall and diaphragm. The specimen was fixed for at least a week in 10 per cent neutral formalin.

METHODS FOR ELECTRON MICROSCOPY

Lung tissue must be fixed within a few minutes of death or of surgical excision if adequate preservation is to be achieved for electron microscopy. Very small pieces cut to about 1 mm. in diameter may be dropped in suitable fixative such as 1 per cent buffered osmium tetroxide (or 2 per cent buffered gluteraldehyde). Alternatively, the fixative may be injected down the airways (Sabatini *et al.*, 1963; Weibel and Knight, 1964) or into the pulmonary arteries (Weibel and Gil, 1968). After two hours the tissue is dehydrated and embedded in Araldite. Gluteraldehyde treatment is followed by post-osmication.

Patches of emphysema in animal lungs can be clamped with forceps after inflation with air, cut off and the forceps immersed in fixative (Boatman and Martin, 1965; Martin and Boatman, 1965).

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2 Present Methods including Measurement of Emphysema

The standard pathological procedure of dissecting tissues in the fresh state and preparing paraffin sections of selected pieces is of little value in studying emphysema. This is because the lungs collapse in an irregular way when they are removed from the chest, and the air-spaces become distorted. Further collapse subsequently occurs when the lung is cut with a knife, since a high pressure and dragging force are required to overcome the toughness of lung tissue. Admittedly, emphysema can be seen sometimes in the subsequent histological sections, but these also show collapse and distortion and it is often difficult to identify air-spaces; certainly their diameters cannot be measured. Also, if the changes of emphysema cannot be seen grossly with reasonable certainty at the time when pieces are selected for histology, the histological appearances may not include diseased parts of the lungs; emphysema is often patchy in distribution.

It is generally agreed that the only satisfactory way to prepare the lungs for demonstrating emphysema is to restore them to their distended state and fix them in that position. Usually it is done by running aqueous formal saline down the bronchi, but in a few laboratories formalin fumes are employed. Fluid fixation has the advantage that it acts as a support during cutting (oedematous lungs cut well even in the fresh state). In either case, distended air-spaces are more distinct on the cut surface of the lung particularly under the dissecting microscope, and in histological sections the fine anatomy is easier to interpret. In the following account, simple refinements in the technique of preparing lung slices are described and the resulting appearances analysed in some detail, since this is a branch of pathology which has received insufficient attention in the past.

PROCEDURE

REMOVAL OF INTACT LUNG

Distension of a lung with fixative cannot be achieved satisfactorily unless the external surface is undamaged. This demands care from an early stage in the necropsy, for the lung is commonly incised accidentally when the costal cartilages are divided. In this respect, a safe method of opening the thoracic cage is to begin by making a hole in the third intercostal space anteriorly by firm pressure and burrowing with a thumb or finger tip, rather than by cutting with a knife which may puncture the visceral pleura. When the lung has fallen back with the entry of air, a knife is inserted carefully into the

hole and the cartilage distal to it is cut in an outward direction at a distance of 1 cm. from the costo-chondral junction. Great care should be taken to keep the lung away from the knife as other cartilages are divided.

It is important not to pull on a lung which is anchored by pleural adhesions, since this almost always strips the visceral pleura from a wide area of the lung, which is very serious, for it cannot be repaired adequately by suturing. Small adhesions can be cut, but extensive adhesions should be bypassed by making an incision in the parietal pleura anteriorly and separating it from the chest wall by extra-pleural dissection with the fingers. If the diaphragm is firmly adherent it should be removed together with the lung; it can be separated from the lung more easily later by dissection after fixation. Exceedingly dense adhesions at the apex of the lung resulting from old tuberculosis may not yield to extra-pleural dissection with the fingers and must be cut. In the absence of adhesions, a long incision in the parietal pleura down each side of the thoracic vertebrae makes it easier to pull the lungs and mediastinal structures away from them. Lastly, when the trachea is opened, care should be taken not to continue the cut and run the scissors down the bronchi. In transecting the hilar tissues to separate the lung, the bronchus and pulmonary artery should be kept long for cannulating.

Small cuts in the lung can be sutured before fixation. Large cuts and tears may render a lung useless for further study.

FIXATION

Distend the lung with fixative as soon as possible after removal from the chest to obtain the best histological preservation. If some delay cannot be avoided, put the lung in a tray, cover it with a damp cloth and place the tray in a refrigerator at 4°C. No fixative should be applied at this stage or the lung will not distend later.

Remove mucus from the major bronchi with a cannula attached to a tap suction pump. Following this, tie another type of cannula in the main bronchus with string. A useful type can be made by mounting a rubber bung with the broad end distally on a glass tube about 8 cm. long, and making a groove round the bung where the string will be tied about the bronchus. An assortment of cannulae should be made with bungs of different sizes to fit the various internal diameters of bronchi tightly. The quality of fixation of the bronchial mucosa is better if formalin is run into the pulmonary arteries instead of, or as well as, the bronchi. Recently, we have cannulated the bronchus and artery routinely, ligating the pulmonary veins. This gets fixative into fibrous areas more efficiently, as well as collapsed areas and tumours. The cannulae are joined by a Y-tube.

The lung is attached to an apparatus (Fig. 2.1) which has been designed to maintain a continuous head of pressure of 25 to 30 cm. of 10 per cent formal saline, collecting back formalin which leaks from the lung (Heard, 1958, 1960, 1962, 1966a; Heard *et al.*, 1967). The pressure should be maintained continuously for a period of at least 72 hours, since formalin fixes slowly. Cover the lung with a thin layer of muslin to keep it moist but not compress it. Lower pressures should be used for the lungs of children (and animals).

In generalized airways obstruction, particularly in the presence of a terminal respiratory infection, part or all of the lung may fail to distend and it will be necessary to raise the pressure to 100 cm. for a few minutes by connecting it to another reservoir. It can be returned to the original pressure when filling is seen to be taking place satisfactorily. However, lungs often fill completely at a slow rate without this procedure and some minutes should be allowed for the lower pressure to have effect.

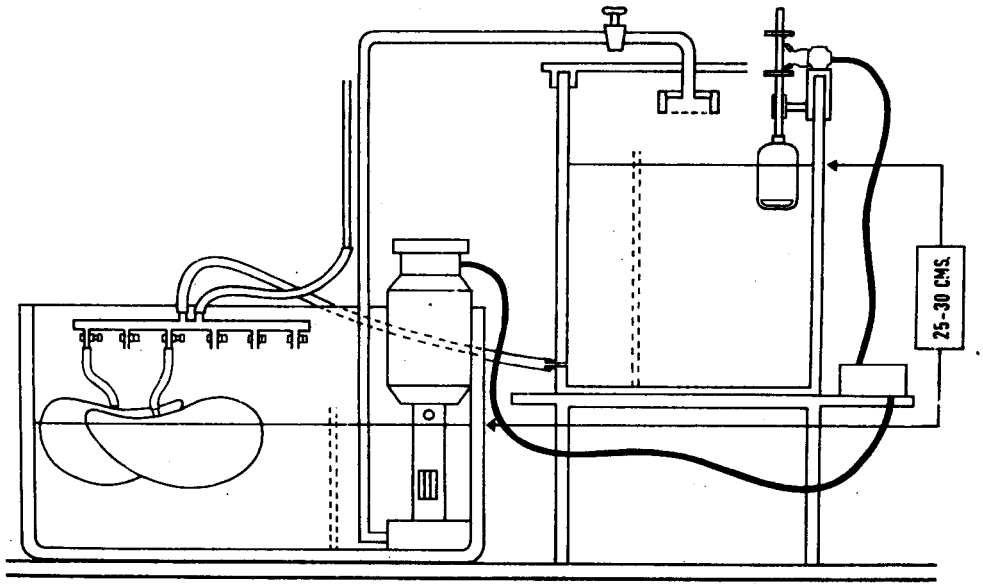

FIG. 2.1. Diagram of apparatus used to maintain distension of the lung during fixation. The centrifugal pump raises formalin to the upper container and is controlled by a float and switches.

MEASURING THE VOLUME OF THE DISTENDED LUNG

A metal tank 25 × 30 cm. and 25 cm. high, fitted near the top with a short syphon, is filled with water. The point at which the syphon stops draining is the required level in the tank. The fixed lung is lowered into the water and pushed to the bottom of the tank with a rod against the hilum. The syphon recommences and all the displaced water is collected and measured in a graduated container. The normal range for volumes of the left lungs of adult males is 1,610 to 3,570 ml. (Heard and Izukawa, 1964) and there is a close correlation between the pathological volume measured in this way and the volume as calculated from the radiograph of the same patient during life (Heard, 1960). Lower readings may be found with severe pulmonary fibrosis, and higher readings are encountered occasionally with severe emphysema.

CUTTING SLICES OF THE LUNG

Place the lung with the hilum upwards on the cutting board, which is made of white Perspex 25 × 30 cm. and fitted with raised edges 8 mm. high down the long edges. A

long very sharp knife is rested on the raised edges and slices are cut from the lung. Stop cutting slices near the middle of the lung to preserve the large bronchi and vessels for subsequent dissection.

Skill is required to obtain well-cut slices. The knife should be particularly sharp and the blade flat and at least 35 cm. long. Use the whole length of the blade, and cut as far as possible through the lung with each stroke, but use only moderate pressure. Keep the knife still between strokes to avoid notching the slice. Prevent the lung from lifting off the cutting board as the last part of the slice is being cut or the slice will be incomplete. Occasionally, calcium is encountered, e.g. healed tuberculosis, and this should be cut with old scissors or bone-cutters before proceeding with the knife.

Severely emphysematous lungs tend to collapse as they are cut, and become distorted. If tap water is run continuously into the bronchial cannula during cutting a better slice is obtained. When emphysema appears so severe from external appearances that the lung is obviously not going to cut well, we have success by prior distension with a hot 1 per cent aqueous solution of agar which is allowed to cool and set.

IMPREGNATING A SLICE OF LUNG WITH BARIUM SULPHATE

A selected slice from the middle of the lung is lightly squeezed free of excess water and placed flat in a tray (25 × 30 cm.) containing saturated aqueous barium nitrate at room temperature for one minute. It is pressed with the finger-tips intermittently to encourage the solution to enter the depths of the slice. After squeezing, it is transferred to a tray of saturated aqueous sodium sulphate for one minute; a cloud of precipitated barium sulphate appears at this stage and the slice quickly whitens. It is then squeezed and washed briefly in running tap water to remove excess barium sulphate. One impregnation is sufficient as a rule. The reagents are used for several weeks and the supernatant is selected each time. The precipitate is retained to strengthen the solution when it is returned to the bottle.

I introduced this method to increase the contrast of alveolar walls in water when a slice of lung is examined in a tray of water. Slices fixed in aqueous formal saline cannot be examined in air because they collapse as the water drains from them, and this occurs very quickly when emphysema is present. In water, the thin alveolar walls (from which blood may have been compressed by pressure-fixation) may be indistinct so that emphysema cannot be excluded with conviction. The method improves the naked-eye clarity of emphysematous lung, and does not mask dust pigment. Slices mounted in museum jars are lighter in colour than usual and more distinct. Similarly, appearances under the dissecting microscope are improved, and photography, particularly at a magnification of 10 × or 20 ×, is greatly facilitated. Over-impregnation should be avoided.

EXAMINING BRONCHI, PULMONARY VESSELS AND LYMPH NODES

After the lateral half of the lung has been sliced the medial half is dissected, commencing at the hilum. Examine the lymph nodes in the loose connective tissue. Open the bronchi

longitudinally with narrow blunt-ended scissors, identifying the distribution of each bronchus beforehand with a round-ended metal probe about 20 cm. long. With distended lung it is often necessary to cut deeply with a scalpel to reach a probed bronchus. Small blunt-ended scissors are required for small bronchi and care is needed not to cut right through both walls and lose the lumen. For general guidance, a diagram of the bronchi is shown in Figs. 2.2 and 2.3.

The pulmonary arteries and veins should be opened *after* the bronchi because they wind round them.

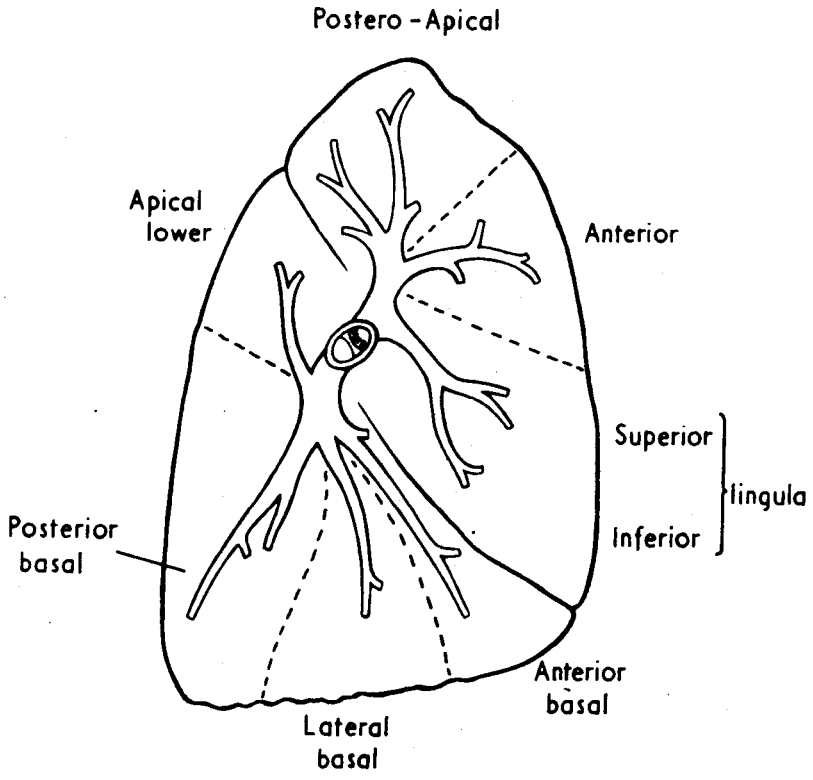

FIG. 2.2. Diagram of the segments and bronchi of the left lung, viewed from the medial side.

MEASUREMENT OF EMPHYSEMA

For many purposes, it is sufficient for the pathologist to state in general terms which parts of a lung are emphysematous, and what type and grade (mild, moderate or severe) each variety takes in those parts. Formidable problems face him when accurate measurements are required, but figures are better for comparing his findings with those of the physiologist. The problems derive from the way in which emphysema varies in

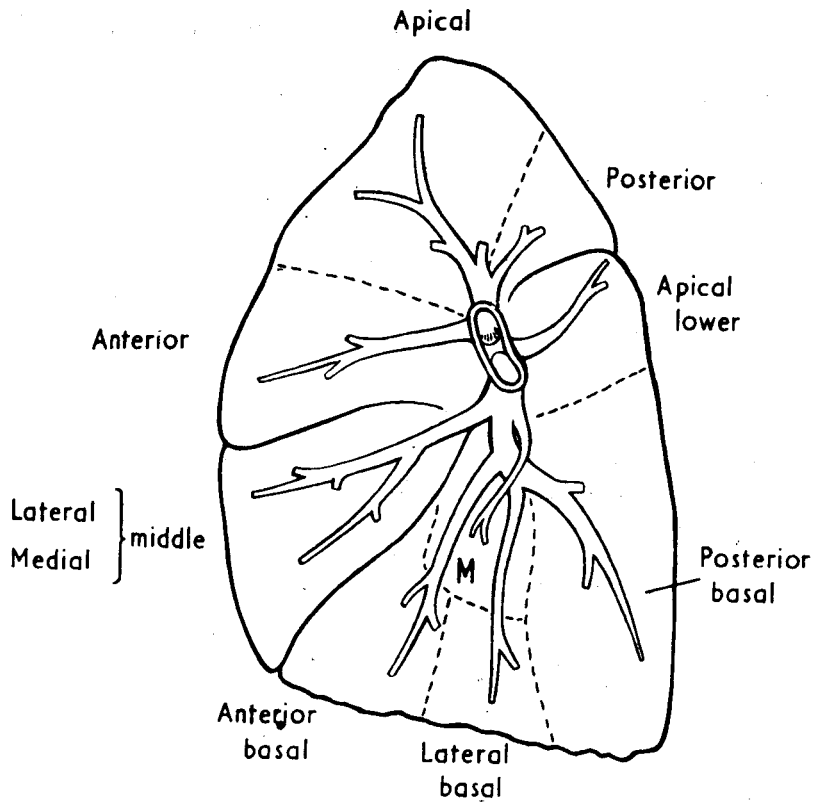

FIG. 2.3. Diagram of the segments and bronchi of the right lung, viewed from the medial side. M indicates the medial basal segment.

type and intensity from one part of the lung to the next, often grading very gradually. Where severe panlobular and centrilobular forms are mixed, the proportion of one or the other in an area may not be recognisable.

Nevertheless, the question has been approached in a variety of ways and several methods are now available which have been found useful for clinico-pathological comparisons. The choice of method depends very much on the time available, and on the limits of accuracy required.

A fast reproducible method which we have used in clinicopathological studies is as follows (Heard and Izukawa, 1964): A prepared slice through the centre of the lung is examined with a dissecting microscope to assess the changes in detail, and then by the naked eye the area is divided visually into 6 regions of equal area (using short metal probes), and each is assessed for emphysema (Fig. 2.4), 1 unit being counted for each one-third of that region which is emphysematous. Half units are also counted. Predominantly distensive emphysema is allotted no more than one unit per region. The result is stated as the number of units counted out of a total of 18 units. An estimate of the percentage of the area of the slice that is emphysematous may be obtained by multi-

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