

News, Notes and Queries

THE EVOLUTION OF BRONCHIAL CASTS

The mammalian lung provides a system of airways in which inspired air is brought into intimate contact with the blood. As well as carrying out this essential physiological function, the hollow structure of the lung has enabled investigators to produce casts of the airways, the study of which has helped in the understanding of air movements within the lung.

The dependence of higher forms of life on air must have been obvious to the ancients. Anaximenes of Miletus (born c. 570 B.C.) stated that air or 'pneuma' (literally 'breath') was essential to life. The function of inspired air was open to some speculation. Plato (428–345 B.C.) stated 'as the heart might easily be raised to too high a temperature by hurtful irritation, the genii placed the lungs in its neighbourhood, which adhere to it and fill the cavity of the thorax, in order that their air vessels might moderate the great heat of that organ, and reduce the vessels to an exact obedience'.

The indefatigable Galen (A.D. 130–199) also interested himself in the function of respiration. It may be that he was the first to have insight into its true nature for he compares it with a lamp burning in a gourd, 'When an animal inspires it is, I think, similar to a perforated gourd, but when respiration is prevented at the appropriate place on the trachea, you may compare it to a gourd unperforated and everywhere closed'.

It seems that these ancient investigators did not concern themselves with the fine structure of the lungs and bronchial tree, and the record of their observations was restricted to simple drawings and woodcuts. But with the fifteenth century came a new interest in art and science which heralded the Renaissance. Anatomy derived great benefit from the more liberal ideas of the period, and the nature of the human body, demonstrated by new techniques, began to be accurately represented by the great artists of the time. One such technique was the use of casts to visualize hollow structures in the human body. Leonardo da Vinci, that 'modern biologist in the guise of a medieval artist' (F. J. Cole) injected melted wax into the ventricles of the brain to demonstrate their structure. His method, while subject to a number of defects, corrected misconceptions evident from his earlier drawings, and provides the first steps in the technique used in this laboratory to produce hollow casts of the bronchial tree nearly 500 years later.

While it appears that Leonardo planned to produce a hollow cast of the cavity of the aorta in its ascending portion, he never applied the technique to the bronchial tree. His ideas on the function of the lungs, which he considered a single organ, are largely due to Galen. About the parenchyma Leonardo writes: 'The substance of the lung is dilatable and extensible. It lies between the ramifications of the trachea in order that those ramifications may not be displaced from their position, and this substance is interposed between these ramifications and the ribs of the chest to act as a soft covering'.

Not surprisingly Leonardo assumed that the total area of cross-section of the ultimate branches of the bronchial tree was equal to the cross-sectional area of the trachea, a misconception not completely corrected until very recently by the use of highly

detailed casts of the bronchial tree and sophisticated mathematical analysis of the nature of airway branching.

The inability of Leonardo and subsequent workers to demonstrate fully the structure of the bronchial tree may be explained in the words of Sir Russell Brock who says: 'Only by a complementary use of bronchial casts or dissections, and of specimens in which the segments are injected separately, can the full story be learned and depicted'.

The use of solidifying injection material, which was a pre-requisite for the production of casts of the bronchial tree, sank into abeyance after Leonardo until it was reintroduced by Jan Swammerdam (1637–1680). He injected a number of organs with wax, though there is no record of his attempting to preserve the bronchial tree in this way. Unfortunately all trace of Swammerdam's preparations have now been lost.

Following Swammerdam's example many materials were tried to discover a suitable solidifying injection, but it was Guillaume Hamberg (1652–1715) who first introduced the injection of alloys. In the *Mémoires de l'Académie des Sciences* (1699) he describes his method of injecting a mixture of equal parts of lead, tin and bismuth which he found would remain liquid at temperatures 'less than was required to scorch paper'. This technique seems to have stimulated an interest in the bronchial tree, for a number of workers, including Govert Bidloo (1649–1713) and William Cowper (1666–1709), attempted to produce metal casts of the air cavities of the lungs. Bidloo claimed that his casts were produced by the injection of molten bismuth, but as Tompsett points out the melting point of bismuth (212°C) is much too high for this to be possible. He probably used an alloy or an amalgam of bismuth. These materials are very brittle, which may explain why none of these preparations has survived. An interesting offshoot of the injection of metals into the lungs was the introduction by Marcello Malpighi (1628–1694), the founder of microscopical anatomy, of mercury injections with which he investigated the structure of the lungs.

The anatomists of the eighteenth century carried these techniques to a high degree of perfection, and while most of their delicate wax corrosion casts have now perished, a record of their existence still remains. In the Royal College of Surgeons of England, there is a portrait of William Hunter (1718–1783) which includes a corrosion cast of the human heart and lungs. Notable among the workers of this period is Thomas Pole who, in 1790, published his textbook of anatomical techniques. His book not only demonstrates his command of anatomical techniques but also offers good advice on the personal qualities necessary for this exacting work. 'In making injections, the principal ingredients, and the first to be obtained, are time and patience, and not less so, a uniform fortitude against disappointments; for it will not infrequently happen that, with the greatest care, a most promising preparation will be instantaneously destroyed by some trivial accident'.

His advice on the 'defence' of casts of the bronchial tree is most sound and especially applicable to casts made of fragile materials such as wax.

Preparations injected for the purpose of corrosion should always be carefully handled, lest the injection be incautiously broke, which, in their finished state having no support from the surrounding vessels, will fall to pieces; this would be an unpleasing circumstance, after everything else had been successfully conducted. . . .

These preparations require great care and much time to complete them, and when finished, are of all others most liable to be demolished by trivial accidents; it is therefore expedient to defend

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them as much as possible from possible injuries . . . for persons who have not made them are not always satisfied with looking, but every now and then trying their strength by the finger, at the expense of destroying its most beautiful parts

Despite the perfection of injection techniques attained by the end of the eighteenth century, there were no significant advances in the subject of bronchial anatomy for a hundred years. In 1880, however, Theodor Aeby published his treatise *Der Bronchialbaum der Säugethiere und des Menschen, nebst Bemerkungen über den Bronchialbaum der Vögel und Reptilien*. In this monument of patient research Aeby carried out measurements on metallic casts obtained from some forty-eight individual species, belonging to fourteen mammalian families. In the section devoted to the human bronchial tree metallic casts were derived from a series of individuals of different sexes, and at various ages including the later foetal months. Unfortunately Aeby's determinations were made exclusively on metallic casts, and while these are capable of great detail they are also liable to serious errors.

It may have been because of these artifacts that he managed to see in the human lung a bronchial stem from which the bronchial tree arose by monopodic branching. Aeby's prestige was so great that his views were generally adopted for some fifty years in spite of the challenge put forward by William Ewart (1848–1929) in *The Bronchi and Pulmonary Blood Vessels* (1889). Ewart confined his investigations to human lungs from which he prepared solid casts of the bronchial tree in low melting point alloy. He injected the isolated lung in the belief that it was Aeby's practice of injecting the lung within the thorax which had led him astray. From consideration of his casts he concluded that the shape of the bronchial tree conforms to the shape of the thoracic cavity, pointing out for the first time how misleading comparisons between the bronchial tree of man and other mammals could be. Ewart also pointed out that the lung could be subdivided into a number of separate anatomical units. He says 'Within each lung large groups of lobules are kept in practical isolation from each other as regards their air supply. Each of these sub-lobar groups may be considered as forming separate respiratory districts'. Ewart's concept of segmental anatomy remained unexploited until after his death when Kramer and Glass in 1932 coined the phrase 'bronchiopulmonary segment' to describe the 'respiratory districts' seen by Ewart in his metal casts some fifty years earlier.

The predecessors of the present-day plastic casts are the cellulose and vinyl resin (Vinylite) casts of Liebow, Hales, Lindshog and Bloomer (1947). Vinylite itself has now been displaced by the cold-setting synthetic unsaturated polyester resins, such as Marco resin. These materials make it possible to produce beautiful, rigid, coloured casts of anatomical cavities. Notable in the use of resins is D. H. Tompsett, who in 1952, described the method of producing resin casts which has been used extensively by morphometrists and other workers wishing to produce solid casts of the bronchial tree up to the present day. Tompsett's original method involved filling the bronchial tree with gelatin and submerging the whole lung in warm water. The gelatin was then displaced from the airways by resin run in through the trachea. When the desired degree of penetration had been attained the gelatin was solidified by pouring iced water over the lung. This prevented further penetration of the resin which was allowed to set. The tissue was then digested away leaving the plastic cast. An alternative method has

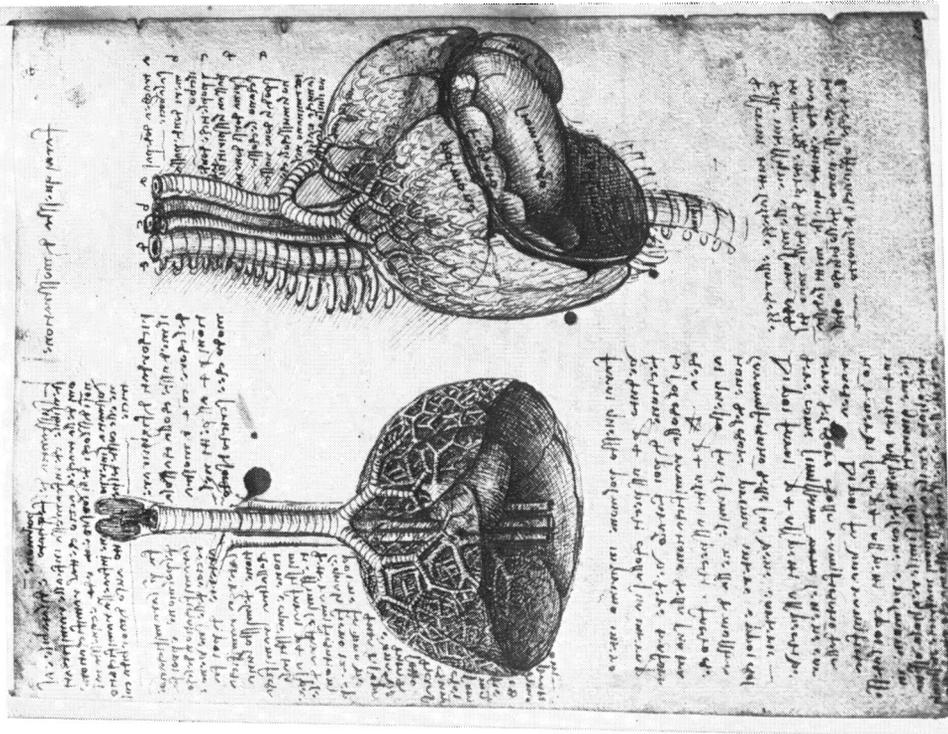


Figure 1
 Drawing of lungs and trachea by Leonardo da Vinci.
 (From Kenneth Clark, *A Catalogue of the Drawings of Leonardo da Vinci at Windsor Castle*, Cambridge, 1935.)

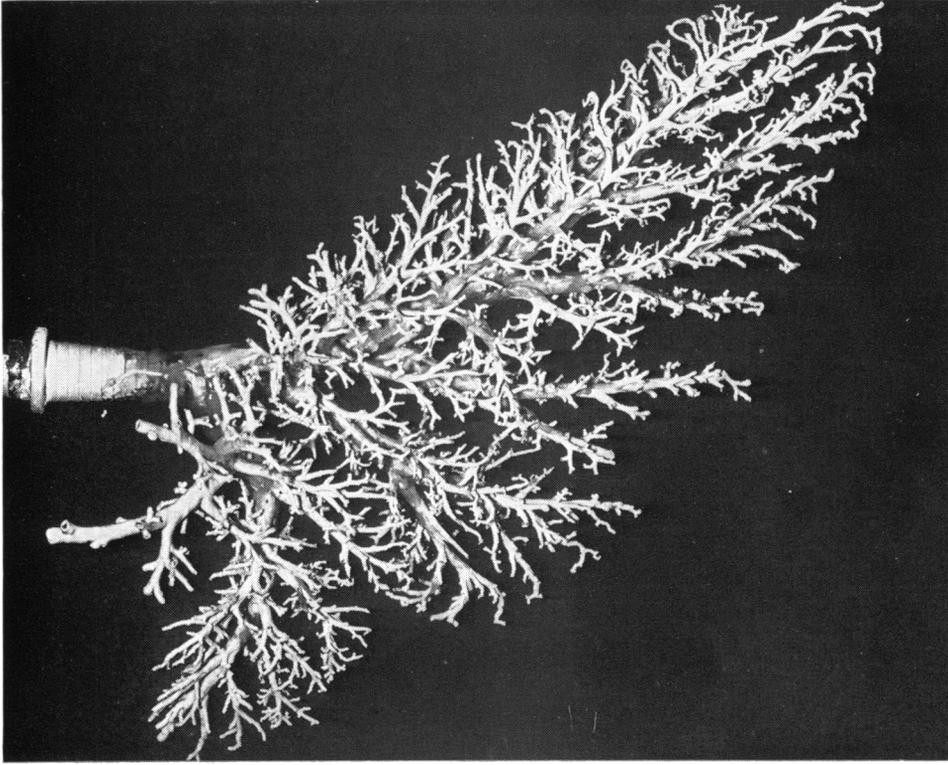


Figure 2
 Hollow cast of pig bronchial tree. Produced by the author.

been described by Rahn and Ross (1957) in which the lungs are dried and fixed in an inflated state by a continuous flow of compressed air through the trachea for two to three days. A polystyrene plastic is poured into the trachea and cured by heating the whole at 80°C for three to six hours.

Solid casts of the air spaces of the bronchial tree have aided, and deceived, anatomists in their investigations of the human lung. An interesting application is the use of measurements made on casts to develop mathematical models of the bronchial tree. These models are then used to predict the nature of gas flow in the lung. No discussion of the use of lung casts for morphometric purposes would be complete without reference to Weibel. His monograph on lung morphometry marked a new era in the subject, and his measurements have been the basis of calculations by many workers of the nature of ventilation in the human lung. Weibel measured all the limbs of a resin cast down to the fifth order of branching, and a sample of the limbs down to the tenth order of branching. From the tenth order of branching to the smaller structures, which he investigated by histological methods, Weibel assumed regular dichotomy and predicted the missing measurements. Because of this the effect of asymmetry in bronchial anatomy was excluded. A number of workers (Rohrer, Findeisen, Hilding and Hilding) have similarly treated the bronchial tree as a symmetrical system. These models demonstrate the idealized state in which all alveoli are equidistant from the carina. Ross (1957) made exhaustive measurements on resin casts of dog lungs and demonstrated that the bronchial tree is in fact an asymmetrical system. Horsfield and Cumming (1968) carried out similar measurements on solid casts of the human bronchial tree. They went on to calculate that the asymmetry they had demonstrated would affect the distribution of ventilation in the lung.

An interesting development in the field of casts of the bronchial tree has been the advent of hollow casts. While these have only been produced in the past twenty years, it is interesting to note that Leonardo proposed to make such a cast of the ascending aorta some 500 years ago. The hollow casts are an obvious step beyond the solid models. For while with solid models only morphometric measurements can be made, and conditions of air flow extrapolated from these, hollow casts are susceptible to direct experimental investigation.

A precursor of the use of hollow casts to investigate flow is seen in the work of E. A. Gaensler, J. B. Maloney and V. O. Bjork (1952). These workers investigated the nature of gas flow in tubes of the same diameter as the human trachea. They discovered that turbulence occurred at much lower flow rates than Rohrer (1915) had calculated from morphometric studies. They established that turbulence probably existed in the bronchial tree at all but the lowest flow rates. The first true hollow cast of the bronchial tree for experimental purposes was produced by West and Hugh-Jones in 1959. These workers took a solid resin cast produced by Tompsett and trimmed all the bronchi distal to the first branching of the segmental bronchi. A flexible hollow cast of the solid model was then produced and a further solid cast made in dental wax. This wax tree was embedded in a block of clear resin with extensions leading from the segmental bronchi to the outside. The wax was melted out leaving a hollow replica of the upper bronchial tree. Patterns of flow were studied by observing the flow of dye in water and different gases through the cast.

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Dekker (1961) produced a similar type of cast of the trachea, with and without the larynx. He used these casts to investigate the effect of the larynx on the onset of turbulence.

A severe limitation on the usefulness of these embedded casts is the small number of airways through which flow can be produced. Access to the innermost airways is blocked by those at the periphery. We (1970) overcame this difficulty by making a hollow cast in which the walls were very thin (0.20 in.) and not enclosed in a block of plastic. This was produced by first making a solid wax cast of the airways when the lung was inflated under negative pressure in an artificial thorax. The tissue was digested off the solid cast in a bath of concentrated hydrochloric acid. A coating of colloidal silver was sprayed over the solid cast to provide a conducting layer and the whole cast silver plated until the walls were of the required thickness. To enable a stream of gas to be passed through the cast the ends of the small bronchi should be open. To ensure this was so, a blob of wax was placed over the colloidal silver at the ends of the bronchi. This prevented electro-plating at these points and when the wax was melted out of the cast these airways were left open.

At about the same time, Eisman produced a hollow lung cast by coating a solid metal cast with latex and then melting out the low melting point metal.

Hollow lung casts provide an attractive alternative to real lungs for placing of instruments such as a hot wire anemometer. Such measurements are being made by Schroter and Sudlow to investigate the velocity profiles across airways of the human lung.

Hollow casts represent a model of the lung 'frozen' at some point in the respiratory cycle. They provide an opportunity to investigate the effect of bronchial tree anatomy on respiratory dynamics without the interfering effect of lung compliance and a gradient of pleural pressure. We have used hollow casts to investigate the deposition of fibres in the lung and to estimate the site of airways resistance. Transit times for a gas front to pass from the carina to small airways has also been measured. In all these investigations the similarity between hollow casts and excised lungs demonstrates the influence of structure on function in the bronchial tree.

The nature of the air spaces within the mammalian lung is of primary importance to its function in health and disease. Over the past three hundred years the understanding of this function has been greatly advanced by the use of solid casts. It is probable that at least as much information can now be gained by the application of experimental techniques to hollow casts, produced by methods outlined five hundred years ago by Leonardo da Vinci.

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LEAD POISONING IN THE ANCIENT WORLD

Lead was one of the seven metals of antiquity. Its discovery dates back to at least 3500 B.C. and lead artefacts have been discovered widespread throughout the ancient world.

Lead does not occur in an elemental state in nature although its sulphide ore galena (PbS) is common. It is probable that galena was first used in antiquity for making into ornaments or for use as an eye paint.¹ The discovery of metallic lead may well have