CHAPTER 1

Anatomy and Physiology of the Pleura

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OVERVIEW

- The pleural space is a real rather than potential space, containing a small amount (<20 mL) of pleural fluid.
- Mesothelial cells line the visceral and parietal pleura, with size and shape varying according to position. They are metabolically active and can perform a variety of functions.
- The parietal pleura is innervated whereas the visceral pleura has no nerve supply (and hence does not produce pain in pathological conditions).
- The pleural space is normally under negative pressure.
- Pleural fluid is secreted from the systemic vessels of the parietal pleura, and is drained through lymphatic channels in the parietal pleura. The normal drainage capacity is very large compared to the secretion capacity.

The pleural cavity is a real rather than potential space, containing a thin layer of fluid and lined with a double-layered membrane covering the thoracic cavity (*parietal* pleura) and outer lung surface (*visceral* pleura) whose precise purpose and structure are incompletely understood. The gaps in our knowledge are best illustrated by the unexplained anatomical variations among different mammals. In humans, the left and right pleural cavities are separated by the mediastinum, but in species as diverse as the mouse and bison there is a single pleural cavity, allowing free communication of fluid and air between right and left. The elephant has evolved to have no cavity at all – instead having loose connective tissue between the two pleural membranes. In time, it may be that describing how and why these differences have evolved will help us to understand the role the pleural cavity has in humans. This chapter focuses on the key features of human pleural anatomy and physiology.

Embryology

The human body contains three mesothelium-lined cavities – two large (pleural, peritoneal) and one small (pericardial) – derived from a continuous mesodermal structure called the intra-embryonic coelom as it is partitioned at 4–7 weeks' gestation. Arising from a medially placed foregut structure that will ultimately form the mediastinum, primordial lung buds grow out into the laterally placed pericardio-peritoneal canals, taking a layer of lining mesothelium that will become the visceral pleura in the process. As the lungs rapidly enlarge, they enclose the heart and widen the pericardio-peritoneal canals to form the pleural cavities. These are separated from the pericardial space by the pleuro-pericardial membranes, whilst the septum transversum (an early partial diaphragm) joins the pleuro-peritoneal membranes to partition each pleural cavity from the peritoneal space. The mesothelium lining the pericardio-peritoneal canals as they become the pleural cavities goes on to form the parietal pleura.

Macroscopic anatomy

The pleura is a double-layered serous membrane overlying the inner surface of the thoracic cage (diaphragm, mediastinum and rib cage) and outer surface of the lung, with an estimated total area of 2000 cm^2 in the average adult male. Between lies the pleural cavity, a sealed space maintained 10–20 micrometres across and filled with a thin layer of fluid to maintain apposition and provide lubrication during respiratory movement. The left and right pleural cavities are completely separated by the mediastinum.

The visceral pleura is tightly adherent to the entire lung surface, not only where it is in contact with chest wall, mediastinum and diaphragm, but also into the interlobar fissures. The parietal pleura is subdivided into four sections according to the associated intrathoracic structures: costal (overlying ribs, intercostal muscles, costal cartilage and sternum); cervical (extending above the first rib over the medial end of the clavicle); mediastinal; and diaphragmatic. Inferiorly, the parietal pleura mirrors the lower border of the thoracic cage but may extend beyond the costal margin, notably at the right lower sternal edge and posterior costovertebral junctions.

The visceral and parietal pleura meet at the lung hilae, through which the major airways and pulmonary vessels pass. Posteriorly, where a double layer of parietal pleura has been pulled into the thoracic cavity during lung development, lie the pulmonary ligaments extending from hilum to diaphragm bilaterally. These are thought to prevent torsion of the lower lobes, and are important intra-operatively as they may contain vessels, lymphatics or tumour.

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Microscopic anatomy

The pleura is composed of a monolayer of mesothelial cells overlying layers of connective tissue; its precise structure varies between visceral and parietal pleura and according to anatomical position. Up to five layers can be identified histologically, consisting of the mesothelial cellular surface and four subcellular layers (basal lamina and thin connective tissue; thin superficial elastic tissue; loose connective tissue containing nerves, vessels and lymphatics; and a deep fibroelastic layer, often fused to the underlying tissue). These subcellular layers tend to be better defined when overlying looser substructures such as the mediastinum, than rigid tissue such as ribs or intercostal muscle. The parietal pleura is approximately 30 micrometres thick and overlies the deeper endothoracic fascia. The visceral pleura is between 30 and 80 micrometres thick with denser connective tissue layers that both contribute to elastic recoil of the lungs during expiration, and protect the lungs during inspiration by limiting their volume and expansion.

Mesothelial cells

The mesothelial cells lining the visceral and parietal pleura are the predominant cell type within the pleural cavity, forming an active multipotent layer capable of sensing and responding to external stimuli. Mesothelial cells dislodged from the pleural surface to float freely within the fluid-filled space can transform into macrophages with immunological roles; whilst various studies have also proven them capable of producing growth factors, extracellular matrix proteins and a range of cytokines. They are metabolically active and have both secretory and absorptive roles, with electron microscopy demonstrating abundant pinocytic vesicles, polyribosomes and mitochondria amongst their intracellular structures. Injury or disruption of the monolayer is repaired through mitosis and migration of adjoining cells or incorporation of free-floating mesothelial cells from pleural fluid.

Their size, shape and surface structure vary subtly according to location within the pleural space, although no major cytological differences have been found between mesothelial cells of pleural, pericardial or peritoneal origin. Each cell has a carpet of microvilli at the pleural surface whose precise role is still unknown; however, the density of microvilli is greatest in the inferior parts of the thorax, and greater in visceral than parietal pleura at corresponding levels. Parietal mesothelial cells in the apices are flatter with fewer microvilli; whilst basally the cells are cuboidal, more numerous per unit area and have a higher density of microvilli. These adaptations may relate to variable lung and chest wall movement at different thoracic levels.

Innervation, blood supply and lymphatics

Innervation

The visceral pleura is innervated by the vagal and sympathetic trunks which do not have pain fibres. Only the parietal pleura contains pain fibres, with pleuritic pain consequently implying involvement of this surface. It is innervated by intercostal nerves and refers pain to the corresponding area of the chest wall; with the exception of the diaphragm which being supplied by the phrenic nerve refers pain to the ipsilateral shoulder.

Blood supply

The parietal pleura is supplied by systemic capillaries according to anatomical location. (Figure 1.1) These originate from the intercostal and internal mammary arteries for the costal pleura; pericardiophrenic artery for the mediastinal pleura; subclavian arteries for the cervical pleura; and superior phrenic and musculophrenic arteries for the diaphragmatic pleura. Venous drainage follows arterial supply into either the superior or inferior vena cava depending on location.

The arterial supply of the visceral pleura is somewhat controversial. It is generally agreed that the bronchial arteries supply the majority of the visceral pleura, although supply of the lung apex and its convex surface is debated and may involve the pulmonary circulation. Venous drainage occurs via the pulmonary veins.

Lymphatics

The visceral pleural lymphatics constitute a superficial network of interconnecting vessels over the surface of and through the lung along the interlobular septae. Lymph flows via the bronchovascular bundles towards the lung hilae, with a greater density of lymphatics in dependent areas of lung with higher intravascular pressures.

Lymphatic plexuses are found in the parietal pleura overlying intercostal spaces, mediastinum and the diaphragm, but are essentially absent over the ribs. The costal pleura drains anteriorly into internal mammary nodes and posteriorly into intercostal nodes at the rib heads. The mediastinal lymphatics drain to tracheobronchial and mediastinal nodes; whilst those in the diaphragm pass to parasternal, middle phrenic and mediastinal nodes.

Whilst the visceral pleura is separate from the pleural space, the parietal pleura is unique in containing stomata that allow direct communication with the underlying lymphatic network and removal of large particles from the pleural space. These stomata are 2–6 micrometres in diameter at rest and found in greatest density in the mediastinum and lower thorax. Beneath the stomata lie dilated spaces called lacunae which drain into the lymphatic network via valves to maintain unidirectional flow. Associated with the stomata in some areas are modified mesothelial cells and immune aggregates

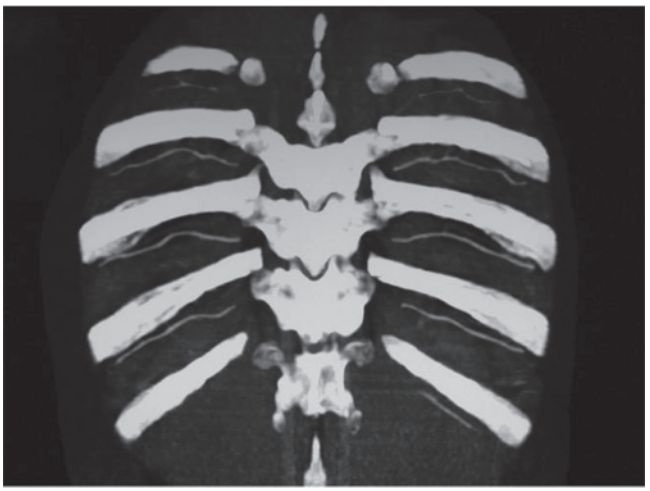

Figure 1.1 CT angiogram demonstrating the course and variability of the intercostal arteries posteriorly.

(lymphocytes, plasma cells and monocytes) surrounding a central lymphatic vessel. These are Kampmeier's foci, thought to have a similar role to Peyer's patches in the gut in local host defence mechanisms.

Physiology of the pleural space

Pleural pressure

The pressure in the pleural space is normally sub-atmospheric, with the tendency of lungs to collapse being countered by the chest wall trying to expand. This negative pressure is not uniform, with a gradient from apex (most negative) to base (least) of more than 8 cm H_2O in an upright position caused by gravity, weight of intrathoracic structures and differences in lung and chest wall shape. This pressure gradient causes different distension pressures in individual lung regions, explaining variation in alveolar size (larger apically) and ventilation (better basally).

Pleural fluid formation and constituents

The volume of pleural fluid in health is small, with mammalian studies placing it between 0.1 and 0.2 mL/kg, whilst a single human study reported a mean volume of 8.4 mL per hemithorax (0.26 mL/kg). This fluid forms a thin continuous film of relatively even thickness (10–20 micrometres) between visceral and parietal pleura.

Pleural fluid is derived from systemic vessels of the pleural membranes, with the vast majority produced by the parietal pleura in the upper thorax. This source fits with anatomical and physiological features of the parietal pleura, with its microvessels being closer to the surface and subject to higher filtration pressures than those of the visceral pleura. Fluid filters from these microvessels through the extrapleural interstitium and into the pleural space down a small gradient. The high-pressure nature of the filtration means pleural fluid has a low protein concentration relative to plasma (approximately 15% of plasma protein levels), with smaller liquid molecules more easily crossing into the pleural space than larger proteins.

However, the electrolyte composition of pleural fluid implies an additional active process in its formation though this has not been identified. Pleural fluid has a greater bicarbonate concentration relative to plasma, and lower concentrations of sodium and chloride. Consequently, pleural fluid is alkaline relative to plasma, with a normal pH of 7.6.

The same human study reported above also informs our knowledge of the cellular content of pleural fluid. This showed a mean of 700 red cells per mm^3 and 1700 white blood cells per mm^3, with the majority of these being macrophages (75%) or lymphocytes (23%). Mesothelial cells, neutrophils and eosinophils make up the remainder. These data are again largely consistent with mammalian studies.

Pleural fluid absorption

Various routes by which fluid exits the pleural space have been proposed, including via capillaries in the visceral pleura or reabsorption by mesothelial cells. It is now accepted that drainage occurs predominantly via lymphatic stomata in the parietal pleura, whose main location in the lower thorax contrasts with the source of pleural fluid production. Support for bulk flow drainage through the stomata rather than membrane diffusion or active transport comes from various factors, including the constant rate of fluid absorption despite variation in protein concentration and ability of comparatively large erythrocytes to leave the pleural space intact. Distal lymphatic flow is influenced by intrinsic vessel contractility and respiratory movements, the latter of which also encourage fluid circulation within the pleural space.

Pleural fluid production and absorption are normally in equilibrium, with their baseline rate estimated to be 0.01–0.02 mL/kg/hour. Should production increase (e.g. during exercise) the rate of drainage responds via a negative feedback mechanism. Studies in patients with heart failure have shown the lymphatic stomata can increase their rate of absorption almost 20-fold, equivalent to over 500 mL/day in the average adult male. This system is extremely effective at regulating pleural fluid volume close to steady-state conditions; it is only once the rate of filtration and production exceeds maximum absorption that pleural effusions occur.

Role of the pleural space

The main function of pleural fluid is to ensure close apposition of visceral and parietal pleura, and allow frictionless movement of these surfaces during breathing. However, there is no evidence for the pleural space itself having an essential role. Human studies on pleurodesis – the intentional obliteration of the pleural space to treat recurrent effusions or pneumothoraces – show no significant impairment of lung function or gaseous exchange post-procedure. Just as we cannot explain variations in pleural anatomy among species, we are unable to answer why the space should exist or have been preserved during evolution.

Further reading

Rahman NM and Wang NS. (2008) Anatomy of the pleura, in *Textbook of Pleural Diseases*, 2nd edn (eds Light RW, Lee YCG), pp.13–36, Taylor & Francis, Boca Raton.