# Fluid balance

Emrys Kirkman

Peter Tryphonopoulos

Christopher Harle

## Abstract

The primary function of the lung is gas exchange between alveolar gas and the blood flowing through the nearby capillaries. This stage of gas exchange takes place by diffusion. Because gases such as oxygen diffuse relatively slowly through liquids it is essential that the fluid barrier is kept as short as possible. Furthermore, it is vital that interstitial fluid does not escape into the alveoli because this would abolish gas exchange in the flooded alveoli and lead to shunt. The net movement of these fluids is largely determined by the Starling forces. A number of physiological mechanisms normally ensure that fluid that does leave the pulmonary microvasculature is quickly removed and hence gas transfer is not impaired. The lungs, in addition, perform a number of other important non-respiratory functions, including modification of circulating levels of a range of biologically active materials, filtration of blood and serving as a reservoir of blood for rapid adjustment of input to the left atrium when needed.

**Keywords** ARDS; lung defences; nitric oxide; pulmonary blood reservoir; pulmonary fluid dynamics; pulmonary metabolism; pulmonary oedema; Starling forces

**Royal College of Anaesthetists CPD Matrix:** 1A01

## Learning objectives

After reading this article you should be able to:

- explain how fluid balance occurs in the lungs and circumstances in which this balance is upset and pulmonary oedema develops
- distinguish between the causes and effects upon pulmonary function of interstitial and alveolar oedema, and how oedema resolves
- describe the role of the airways in protection from inhaled particles, and how the site and mechanism depend upon particle size
- outline important non-respiratory functions of the lung, including filtration and metabolic roles of the pulmonary vasculature, and its value as a blood reservoir

## Movement of fluid across the capillary wall and its removal by lymphatic drainage

The forces and principles that govern the exchange of fluid between plasma within the pulmonary microvasculature and the interstitium are collectively called the Starling forces. They are discussed in detail by Waterhouse et al.[1]

**Osmosis** refers to the diffusion of solvent molecules (i.e. water) across a semi-permeable membrane, from a region of low to high solute concentration. The pressure necessary to prevent this solvent migration is referred to as the **osmotic pressure**.

The osmotic pressure is proportional to the concentration of solutes in solution, and this concentration of osmotically active particles is conveyed as **osmoles**. **Osmolarity** and **osmolality** refer to the number of osmoles per litre of solution or kilogram of solvent, respectively.

**Tonicity** describes the relative solute concentrations between two solutions separated by a semi-permeable membrane. It encompasses the nature of the semi-permeable membrane, as well as the solutes that are unable to diffuse across it (i.e. the effective solutes), and excludes those that freely do so. In clinical practice, tonicity describes the osmolality of a solution as compared to plasma (and specifically, in reference to the cell membrane). Intravenous fluids can thus be categorized as hypertonic, isotonic, or hypotonic (to plasma).

Colloids are large-molecular-weight solutes in solutions. Plasma proteins are the major colloids present in plasma. The **oncotic pressure** (or colloid osmotic pressure) refers to the colloid contribution to the total osmotic pressure of a solution. Because colloids do not easily cross cell membranes, they are important in capillary fluid dynamics.

The Starling forces are classically divided into either hydrostatic or osmotic pressures. The forces dictating the movement of fluid out of the capillary involve the capillary hydrostatic pressure (which forces fluid out of the capillary), and the interstitial oncotic pressure (the osmotic pressure that draws water into the interstitium). These are opposed by their counterparts, the interstitial hydrostatic pressure and plasma oncotic pressure. Fluid movement depends not only on the sum of these forces, but also on the permeability ('leakiness') of this capillary membrane. Permeability to water and to protein will enhance the movement of fluid out of the capillary by, respectively, allowing water to flow out more easily and by diminishing the ability of the plasma proteins to oppose outward movement of water. More recent research has demonstrated the importance of the endothelial glycocalyx, a network of membrane-bound gel-like proteins on the endothelial luminal surface, which provides a primary barrier to fluid and solute exchange.

The plasma oncotic pressure is thought to be approximately 28 mmHg. There is marked variation in capillary hydrostatic pressure, with the highest pressures found in the dependent parts of the lung. Interstitial hydrostatic pressure contributes to the

***Emrys Kirkman*** *PhD is a Principal Physiologist in Biophysics and Trauma (Surgical Sciences) at Dstl, Porton Down, and is an Honorary Senior Lecturer in Physiology at the University of Durham and James Cook University Hospital, Middlesbrough, UK. Conflicts of interest: none declared.*

***Peter Tryphonopoulos*** *MD is a Resident in the Department of Anesthesia and Perioperative Medicine at Western University, London, Ontario, Canada. Conflicts of interest: none declared.*

***Christopher Harle*** *MBChB FRCA FRCPC is a Consultant Anaesthesiologist in the Department of Anesthesia and Perioperative Medicine, Western University, London, Ontario, Canada. Conflicts of interest: none.*





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effect of drawing fluid out of the capillary, and is thought to be slightly negative (5–7 mmHg) by many workers, although some believe it to be slightly positive. The capillary wall is permeable to water and small ions, but restricts the movement of proteins (reflection coefficient 0.7). This is measured on a scale of 1 (totally impermeable to proteins) to 0 (freely permeable to proteins).[1]

Recent evidence suggests that there is a regulated 'leak' of albumin out of the pulmonary capillary in the normal lung, by means of a transcellular pathway involving transcytosis of albumin via caveolae (invaginations of the plasma membrane) in the endothelial cells. The function of this process is to maintain the hydration of the interstitium. It is a closely regulated process and the albumin is eventually cleared via the lymphatic system. This is in marked contrast to the unregulated increase in protein permeability of the endothelial barrier during inflammation when much greater amounts of protein leak owing to increased gaps between cells.

The net effect of the Starling forces across the pulmonary capillary endothelium is a net outward movement of water into the interstitium. This water, along with any accompanying excess solutes, must be cleared by the lymphatic system to avoid interstitial fluid buildup and tissue oedema. Histologically, it is often found that the interstitium is wider on one side of the capillary than on the other (where the barrier between the alveolar air and capillary blood is extremely thin). It is the wider interstitium that is thought to be the most important for fluid exchange in the lungs. There are no lymphatic vessels in this part of the lung, so the newly formed interstitial fluid tracks along the interstitium to the perivascular and peribronchial areas, which form a thin sheath around the arteries, veins and bronchi. Here, the fluid enters lymphatic vessels and is pumped by these vessels towards the bronchial and hilar nodes. It is estimated that pulmonary lymph flow is approximately 20 ml/hour. Any remaining fluid that is not removed by the lymphatic vessels at this stage tracks onwards to the loose interstitial tissue.

Lymph flow can be impeded by iatrogenic as well as disease processes. Mechanical ventilation and positive end-expiratory pressure (PEEP) can impede lymph flow by increasing intrathoracic pressure. Furthermore, increases in intra-abdominal pressure can also impede lymph drainage and contribute to the development of pulmonary oedema, leading to secondary respiratory failure upon mechanical ventilation with high intrathoracic pressure.

## Alveolar water

There is normally very little movement of fluid from the interstitium into the alveolar space, because the epithelium forming the wall of the alveoli represents a very 'tight' barrier that prevents the movement of small ions. Any fluid that does enter the alveoli or small airways is removed via a mechanism that depends on active transport of sodium. Sodium channels are present in the apical surface of the epithelial type II cells. Sodium therefore diffuses into the cells from the fluid in the alveoli down a concentration gradient maintained by the $N^+$, $K^+$-ATPase in the basolateral membrane of the epithelial cells, which pumps $Na^+$ into the interstitial fluid. There is some recent evidence that epithelial type I cells also participate in this process. The resultant movement of $Na^+$ generates a mini-osmotic effect, which in turn drives the movement of water from the alveoli/small airways into the interstitium.

## Pulmonary oedema

Despite the alveolar capillary barrier being very thin, because it is very strong, normally little fluid leaks from the interstitium to alveolar spaces. Type IV collagen within the extracellular matrix augments this but when fluid does escape it is returned via sodium mediated active transport. The apical surfaces of epithelial type II cells contain channels that enable sodium to travel down its concentration gradient. This is further augmented by epithelial type I cells. Consequently a chain of events sees sodium movement promote mini-osmosis leading to egress of water from areas critical to normal gas exchange back to the interstitium and thence to the pulmonary capillaries.

Pulmonary oedema is explicable in terms of deranged Starling forces. Simple elevation of hydrostatic pressure will facilitate capillary fluid loss. However if this is sustained an observable oscillation in endothelial intracellular calcium levels is thought to result in production of oxygen free radicals and thereby an inflammatory like response. This results in excessive permeability, breach of the endothelial barrier and alveolar fluid spillage.

The Starling forces can be modified in a range of clinical conditions.[1] Of principal concern in the lung are factors that increase the rate of fluid movement out of the capillaries, which can lead to pulmonary oedema. Clinically relevant examples are given in Table 1.

A sustained increase in pulmonary hydrostatic pressure increases fluid efflux, which would be expected merely as a consequence of the increased outward-driving hydrostatic pressure. However, recent evidence suggests a more complicated picture because sustained elevations of capillary hydrostatic pressure (in the clinically relevant range) have been shown to elevate endothelial intracellular calcium levels (or oscillations in

### Causes of pulmonary oedema

| Mechanism | Participating event |
|---|---|
| Increased capillary hydrostatic pressure | Myocardial infarction, mitral stenosis, fluid overload, pulmonary veno-occlusive disease |
| Increased capillary permeability | Inhaled or circulating toxins, sepsis, radiation, oxygen toxicity, ARDS |
| Reduced lymph drainage | Increased central venous pressure, lymphangitis carcinomatosa |
| ?Decreased interstitial pressure | Rapid removal of pleural effusion or pneumothorax, hyperinflation |
| Decreased colloid osmotic pressure | Overtransfusion hypoalbuminaemia, renal disease |
| Uncertain aetiology | High altitude, neurogenic overinflation, heroin |

ARDS, acute respiratory distress syndrome.
From West JB. Pulmonary physiology and pathophysiology. Baltimore/Philadelphia (USA): Lippincott Williams & Wilkins, 2001.

**Table 1**




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