# Management of Acute Pulmonary Edema in the Intensive Care Unit

**An Essay**

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in Intensive Care

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*Candidate*

**Maie Marouf**

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# List of Abbreviations

| Abbr. | Full-term |
|---|---|
| **ACC/AHA** | : American College of Cardiology Foundation / American Heart Association. |
| **ACEI** | : Angiotensin converting enzyme inhibitor. |
| **ADHF** | : Acute decompensated heart failure. |
| **AE** | : Alveolar epithelium. |
| **ALF** | : Alveolar lining fluid. |
| **ALI** | : Acute lung injury. |
| **APE** | : Acute pulmonary edema. |
| **APRV** | : Airway pressure release ventilation. |
| **ARBs** | : Angiotensin II receptor blockers. |
| **ARDS** | : Acute respiratory distress syndrome. |
| **ASIC2** | : Acid-sensing ion channel 2. |
| **ASL** | : Airway surface liquid. |
| **AT** I | : Alveolar type I. |
| **AT** II | : Alveolar Type II. |
| **BiPAP** | : Bilevel positive airway pressure. |
| **BNP** | : Brain natriuretic peptide. |
| **BUN** | : Blood urea nitrogen. |
| **CF** | : Cystic fibrosis. |
| **CFTR** | : Cystic fibrosis transmembrane conductance regulator. |
| **CPAP** | : Continuous positive airway pressure. |
| **CPE** | : Cardiogenic pulmonary edema. |
| **CT** | : Computed tomography. |
| **ECG** | : Electrocardiogram. |
| **EELV** | : End-expiratory lung volume. |
| **ENa$^+$C** | : Epithelial sodium channel. |
| **FRC** | : Functional residual capacity. |
| **HACE** | : High altitude cerebral edema. |
| **HAPE** | : High altitude pulmonary edema. |

# List of Abbreviations *(Cont.)*

| Abbr. | Full-term |
|---|---|
| **HFSA** | : Heart Failure Society of America. |
| **IABP** | : Intra-aortic balloon pumping. |
| **IRV** | : Inverse ratio ventilation. |
| **IV** | : Intravenous. |
| **LV** | : Left ventricle. |
| **MCP**-1 | : Monocyte chemoattractant protein-1. |
| **MSCs** | : Mesenchymal stem cells. |
| **NCPE** | : Non-cardiogenic pulmonary edema. |
| **NIV** | : Non-invasive ventilation. |
| **NO** | : Nitric oxide. |
| **NPE** | : Neurogenic pulmonary edema. |
| **NPSV** | : Non-invasive pressure-support ventilation. |
| **NTG** | : Nitroglycerin. |
| **PA** | : Pulmonary artery. |
| **PAC** | : Pulmonary artery catheterization. |
| **PCL** | : Peri-ciliary liquid. |
| **PCWP** | : Pulmonary capillary wedge pressure. |
| **PDIs** | : Phosphodiesterase inhibitors. |
| **PE** | : Pulmonary edema. |
| **PEEP** | : Positive end-expiratory pressure. |
| **PIP** | : Peak inspiratory pressure. |
| **$P_{TM}$** | : Transmural pressure. |
| **RAGE** | : Receptor for advanced glycation end-products. |
| **SP-A** | : Surfactant proteins A. |
| **SP-D** | : Surfactant proteins D. |
| **SVR** | : Systemic vascular resistance. |
| **VAP** | : Ventilator-associated pneumonia. |
| **VILI** | : Ventilator-induced lung injury |

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# Introduction

Acute pulmonary edema is one of the most common life-threatening medical emergencies, that requires immediate intervention with management plan and evidence-based treatment protocol as soon as the diagnosis is suspected, to ovoid its complications ***(Baird et al., 2010).***

The alveolar–capillary membrane exists in the gas exchanging region of the lungs, it is extremely thin to allow sufficient oxygen diffusion, yet it is extremely strong also. Any mechanical injury to the alveolar-capillary membrane resulting from an abrupt rise in the pulmonary capillary hydrostatic pressure, or increase in the pulmonary capillary permeability will lead to acute pulmonary edema ***(Kindlen, 2003).***

Acute pulmonary edema is defined as fluid accumulation in the air spaces and parenchyma of the lungs, that leads to impaired gas exchange and may cause respiratory failure ***(Ware and Matthay, 2005).*** The incidence of pulmonary edema differs according to the causes, sex and increases with age and may affect about 10% of the population over the age of 75 years ***(Patton and Baker, 2000).***

It is generally classified into two main pathogenetic types: hydrostatic (commonly cardiogenic), also termed hemodynamic or high pressure pulmonary edema, and the other

is increased permeability (noncardiogenic) pulmonary edema ***(Bernard et al., 1994).*** Hydrostatic pulmonary edema is caused by acute excerbation of congestive cardiac failure as occurs in myocardial infarction, hypertension, arrhythmias, and high fluid or salt intake**.** Many causes are responsible for non cardiogenic pulmonary edema, such as adult respiratory distress syndrome, neurogenic causes, and high altitude pulmonary edema ***(Ware and Matthay, 2005).***

Diagnosis of acute pulmonary edema depends on history, symptoms, and signs. The symptoms may start as a primary manifestation of a certain condition or as evolution of an existing condition. Laboratory tests such as analysis of arterial blood gases and radiological findings such as in chest x-ray and echocardiography are helpful in diagnosis. In some cases pulmonary artery catheterization may be used ***(Patton and Baker, 2000).***

Pulmonary edema should be differentiated from other causes of dyspnea such as bronchospasm, exacerbation of chronic obstructive pulmonary disease(COPD), pulmonary embolism, myocardial infarction, and acute oliguric renal failure. Possible complications that could occur from pulmonary edema are acute heart attack, cardiogenic shock, arrhythmias, electrolyte disturbances, mesenteric insufficiency, respiratory arrest, and death ***(Patton and Baker, 2000).***

When a patient is in respiratory distress, the initial treatment should occur at the same time or even before the diagnosis is made. Oxygen is the first drug. Other used drugs are: intravenous diuretics like furosemide, nitroglycerin and captopril. Morphine may help with the feeling of shortness of breath. Mechanical ventilation is needed in cases of respiratory failure. When the case is established, the underlying cause of pulmonary edema needs to be diagnosed, and this will direct further therapy ***(Bersten, 1995).***

A key component in the management of acute pulmonary edema is postacute care which presents an opportunity to optimise wellbeing and prognosis through definition of problems, education and support of the patient for changing his lifestyle ***(Baird et al., 2010).***

# Functional Anatomy of the Alveolar-Capillary Interface

The lung surface of air-breathing vertebrates is formed by a continuous epithelium that is covered by a fluid layer. In the airways, this epithelium is largely pseudostratified consisting of diverse cell types, whereas the alveolar epithelium consists of alveolar type I and alveolar type II cells ***(Coppens et al., 2007).***

Regulation and maintenance of the volume and viscosity of the fluid layer covering the epithelium is one of the most important functions of the epithelial barrier that forms the outer surface area of the lungs. Therefore, the epithelial cells are equipped with a wide variety of ion transport proteins, among which $Na^+$, $Cl^-$, and $K^+$ channels have been identified to play a role in the regulation of the fluid layer. Malfunctions of pulmonary epithelial ion transport processes and; thus, impairment of the liquid balance in our lungs is associated with severe diseases, such as cystic fibrosis and pulmonary edema ***(Finger et al., 2003).***

## A) Pulmonary epithelium:

### 1. Composition of the pulmonary epithelium:

In all surface epithelia of the conducting airways, various cell types can be found, which consist mainly of ciliated cells, clara cells, undifferentiated basal cells, and goblet cells.

These cells are expressed in different proportions in the airway epithelia (nasal, tracheal, bronchial), and their local distribution, the frequency of ciliated cells increases progressively towards the periphery, the number of basal cells decreases progressively more distally, and non-ciliated cells are also unequally distributed ***(Coppens et al., 2007).***

Additionally epithelial serous cells are more abundant than goblet cells. The single cell types may also vary in their ultrastructural features between different species, as shown for the microvilli-containing bronchiolar epithelial clara cells ***(Kim et al., 2007).***

Ciliated cells are known to be responsible for the transport of inhaled particles and the mucous layer in the oral direction by beating of their motile cilia. Most airway epithelial cell types such as ciliated cells, clara cells, and goblet cells secrete ions, phospholipids, mucus, surfactant, and immunoprotective proteins such as the clara cell secretory protein ***(Coppens et al., 2007).*** Basal cells are undifferentiated and serve as stem cells for other airway epithelial cell types like ciliated cells ***(Rock et al., 2009).***

## 2. Mucociliary Clearance and Airway Lining Fluid:

An intact mucociliary clearance is essential for a healthy lung and is a part of the innate immune system. It is responsible for cleaning the airways from inhaled pathogens and particles. Its function is mainly dependent on two

parameters: ciliary beat and ion transport. Thus, the ciliated cells occupy an essential role in the mucociliary clearance because of the coordinated beating of their cilia and the set of ion channels they express ***(Song et al., 2009).***

The variety of ion-absorbing and ion-secreting mechanisms enables the airway epithelial cells to control transepithelial water flow and, thus, to regulate the composition of the periciliary liquid (PCL) surrounding the cilia for optimal ciliary beat ***(Boucher, 2002).***

The PCL together with the mucous layer that covers the PCL forms the airway surface liquid (ASL) **(Figure 1).** The mucous layer with all its trapped particles and pathogens is transported orally by the ciliary beat and by that forms an important part of the innate immunity of the lung. Thus, severe effects such as respiratory infections are observed when ciliary beat is impaired due to defects in its regulation ***(Olbrich et al., 2002).***

Additionally, the ASL of the conducting airways represents an important part of the innate immunity, because it contains immunoreactive proteins, such as the clara cell secretory protein as well as the surfactant proteins A (SP-A) and D (SP-D) that are secreted by the airway epithelial cells ***(Kim et al., 2007).*** The endogenous function of clara cell protein is not fully understood, but it is thought to have immunomodulatory functions. SP-A and SP-D play an