Introduction

Acute respiratory distress syndrome (ARDS) is a life threatening respiratory condition characterized by hypoxemia and stiff lungs without mechanical ventilation, most patients would die **(Tortorella et al., 1999)**.

The incidence of ARDS is quoted to be between 17 and 34 per 100 000 patients per year. About 16% of all patients ventilated in the intensive care unit (ICU) for 24 h or more develop ARDS. These patients have a high mortality. This is a reflection of the severity of the primary pathology causing ARDS, other associated organ failures, and complications associated with critical illness (**McCallum & Evans , 2005)**.

ARDS represents a stereotypic response to many different inciting insults and evolves through a number of different phases: alveolar capillary damage to lung resolution to a fibro-proliferative phase. The pulmonary epithelial and endothelial cellular damage is characterized by inflammation, apoptosis, necrosis and increased alveolar-capillary permeability, which lead to development of alveolar edema **(Ware & Matthay , 2000)**.

Since its first description in 1967 **(Ranieri et al., 2012)**, there have been a large number of studies addressing various clinical aspects of the syndrome (risk factors, epidemiology,

treatment) as well as studies addressing its pathogenesis (underlying mechanisms, biomarkers, genetic predisposition). A search of PubMed using the search terms: "Acute Respiratory Distress Syndrome" yields >20,000 journal articles. However, despite this intense research activity, there are very few effective therapies for ARDS other than the use of lung protection strategies. This lack of therapeutic modalities is certainly related to the complex, pathogenesis of this syndrome with multiple signaling pathways activated depending on the type of lung injury. In addition, the lack of sensitive and specific diagnostic criteria to diagnose ARDS has hampered progress. To partially address the latter concern a recent consensus group made a number of changes to the previous American-European Consensus Conference definition of ARDS **(Ranieri et al., 2012)**.

Acute lung injery (ALI) and ARDS are diseases of altered capillary permeability characterized by significant fluid imbalances and oncotic pressure changes. Although investigations directed at these abnormalities may improve patient-centered outcomes, fluid management in ALI/ARDS continues to be a source of great controversy. In this present study, we discuss fluid balance and the colloid osmotic pressure gradients in ALI/ARDS **(Rivers et al., 2001).**

In the early phase of ARDS, an associated septic state is usually responsible for hypovolemia. At this stage, hemodynamic optimization by early and adapted fluid loading has proven its prognostic value **(Rivers et al., 2001)** and a fluid restriction strategy can result in hemodynamic aggravation and dysfunctions of associated organs, determining the mortality of patients with ARDS **(Stapleton et al., 2005)**. Subsequently, hemodynamic stabilization is generally associated with a resumption of diuresis and a decrease in body weight. Passage from one phase to another often is complex and difficult to distinguish but it is probably by identifying the transition between these two phases that one can detect the moment when a strategy of optimization of fluid balance on the restrictive side is possible **(Stapleton et al., 2005)**.

Fluid management is one of the most difficult measures to manage in septic shock patients with ARDS.

A conservative fluid management strategy maintaining a relatively low central venous pressure is associated with the need for fewer days of mechanical ventilation compared with a liberal fluid management strategy in ARDS **(Wheeler , 2006)**. However, conservative fluid management is highly recommended after hemodynamic stabilization in ARDS patients. In hemodynamically unstable patients, dynamic

monitoring of lung fluid balance needs to be implemented to guide the administration of fluids in ARDS patients **(Huh & Koh , 2013)**. Despite a putative beneficial role in the resolution of alveolar edema seen in preliminary studies, recent evidence has indicated significant detrimental effects associated with beta-2 agonist use in ARDS patients **(Gao Smith et al., 2012)**.

Aim of Review

This review is going to discuss ARDS as one of the main life threatening complications of ICU patients and the recent approaches of fluid management in cases of Acute Lung Injury and ARDS which aims to reduce the period of the patient's stay in ICU and decrease morbidity and mortality in ICU.

Review of Literature

Historical Background and Definitions

There are many interesting historical events that correlated with or impacted the identification and management of ARDS leading to the most current concepts. These events set the stage for the critical care revolution that occurred in the last half of the twentieth century.

In 1821, in what was probably the first published scientific description, Laennec described the gross pathology of the heart and lungs and described idiopathic anasarca of the lungs; pulmonary edema without heart failure in "A Treatise on Diseases of the Chest **(Phua et al., 2008)**.

By the 1950s, pulmonary edema had become a medical subject heading by the National Library of Medicine; however, no distinction was made at that time between cardiac and noncardiac causes. But what clearly moved ARDS from a nearly universally fatal form of "double pneumonia" was the development of methods of establishing secure airway access using tubes that could be attached to mechanical ventilators to deliver adequate pulmonary distending pressures **(Adhikari , 2010)**. These techniques extended the lives of these patients from a few hours to many days or even weeks—long enough to

recover in some cases. As this new kind of patient began to populate the newly established intensive care units, their condition rapidly became recognized as one of the most challenging acute clinical processes to treat. Since acute, diffuse, and dense bilateral infiltrates were almost never observed except in patients requiring prolonged mechanical ventilation, many surmised the cause of such infiltrates was the ventilator, hence the term "respirator lung" **(Bernard, 2005) .**

For a period of time ARDS went by the name of inciting injuries (e.g., DaNang lung, shock lung, post-traumatic lung, etc.). It wasn't until 1967, in a landmark article published in Lancet, that Ashbaugh, Bigelow, Petty, and Levine first described the clinical entity that they called "acute respiratory distress in adults" **(Bernard, 2005)**.

This article recognized for the first time that ARDS was a constellation of pathophysiologic abnormalities common to a relatively large number of patients but that were initiated by a wide variety of unrelated insults—for example, gastric aspiration, sepsis, blunt trauma, near-drowning, etc. Interestingly, the difficulty in making the diagnosis remained evident in that at least five of the patients studied could have had ARDS secondary to or complicated by fluid overload.

Also notable in this 1967 report, ARDS was "acute" respiratory distress syndrome. However, in 1971 Petty and Ashbaugh used the term "adult" respiratory distress syndrome in another publication, probably to address the perception of ARDS as an adult version of the previously described infant respiratory distress syndrome (IRDS) **(Murray et al., 2012)**.

In 1992 the American European Consensus Conference (AECC) was charged with developing a standardized definition for ARDS to assist with clinical and epidemiologic research. The AECC recommended that a new designation, acute lung injury (ALI), be defined as "a syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension" and "is associated most often with sepsis syndrome, aspiration, primary pneumonia, or multiple trauma and less commonly with cardiopulmonary bypass, multiple transfusions, fat embolism, pancreatitis, and others." Acute (not adult) respiratory distress syndrome was defined as a subset of ALI patients with more severe oxygenation defect. ALI and ARDS are acute in onset and persistent, associated with one or more known risk factors, and are characterized by arterial

hypoxemia resistant to oxygen therapy alone and diffuse radiologic infiltrates **(Bernard, 2005)**.

In 1994, a new definition was recommended by the American–European Consensus Conference Committee (AECC) which was defined as severe dyspnea, tachypnea, cyanosis refractory to oxygen therapy, decreased pulmonary compliance, and diffuse alveolar infiltrates on chest radiography **(Spragg et al., 2010).**

The consensus recognizes that patients with ARDS when they had severe hypoxemia (PaO_2/FiO_2 ratio < 200), patients with less severe hypoxemia (PaO_2/FiO_2 ratio ≤ 300) are considered to have ALI **(Bernard, 2005).**

ARDS is considered the most severe form of acute lung injury (ALI);

Matthay et al., Stated that the definition of ARDS is a syndrome of inflammation and increased permeability of pulmonary tissue that is associated with constellation of clinical, radiological and physiological abnormalities that cannot be explained by left atrial or pulmonary capillary hypertension **(Matthay et al., 2012).**

Bongard et al., described the character of ARDS, which formed from:

1. The condition should be of acute onset.

2. The deficit in oxygenation should Pao_2/Fio_2<200 mmHg irrespective of PEEP therapy.

3. A frontal chest radiograph should show bilateral infiltrates.

4. The pulmonary artery occlusion pressure should be < 18 mm Hg without any evidence of left atrial hypertension.

Delphi Definition of ARDS

Ferguson et al., modified the AECC definition of ARDS to improve the accuracy of diagnostic criteria. This modification included Pao_2/Fio_2 ratio of ≤ 200 mmHg with a PEEP of ≥10, recording the risk factor, and decreased static compliance **(Raghavendran & Napolitano, 2011)**.

EPIDEMIOLOGY AND INCIDENCE

Before the advent of intensive care, patients with ARDS did not live long enough for organized investigations. With better descriptors of the process of ARDS and the need to have a better understanding of the public health burden, the National Institutes of Health (NIH) organized a workshop in 1977 **(MacCallum & Evans, 2005)**. Among other issues discussed was the estimated incidence of ARDS in the United States. By report of many of those who attended, the estimate of 150,000 cases per year in the United States was mostly just a guess, yet that figure has become widely cited. The actual incidence has

now been approached more systematically and estimates range from about 15,000 to as high as 200,000 cases per year **(Force, 2012).** A recent report by Luhr and coworkers **(Villar et al., 2011)** perhaps explains the problem involved in making precise estimates. These investigators found that among patients requiring mechanical ventilation for more than 24 h, for every patient with a diagnosis of ARDS there were roughly 10 other patients with hypoxemic respiratory failure. This latter group is very important from a public health perspective but is poorly described. It is likely that much of the variation in incidence rates relates to the difficulties in standardizing the radiologic diagnosis **(Force, 2012)**.

Pathology

The characteristic pathological findings in the lungs of patients with ARDS were best described in a classic study in 1977 that included ultrastructural details at different time points in the acute, subacute, and chronic phases (**Figure 1**) **(Matthay& Zemans, 2011).**

In the acute phase (the first 1– 6 days), there is evidence of interstitial and alveolar edema with accumulation of neutrophils, macrophages, and red blood cells in the alveoli **(Figure 1 a, b)**. There is also evidence of both endothelial and epithelial injury, often with denuding of the alveolar epithelium **(Figure 1c)**. There are prominent hyaline membranes in the alveoli as well **(Figure 1b) (Matthay & Zemans, 2011).**

In the subacute phase (the next 7–14 days), some of the edema has usually been reabsorbed, and there is evidence of attempts at repair with proliferation of alveolar epithelial type II cells. There may also be infiltration of fibroblasts and some evidence of collagen deposition. **(Matthay & Zemans, 2011).**

In the chronic phase (after 14 days), there is resolution of the acute neutrophilic infiltrate (unless there has been superimposed nosocomial pneumonia) with more mononuclear cells and alveolar macrophages in the alveoli, and often more fibrosis with ongoing evidence of alveolar epithelial repair. In

many patients, resolution progresses without fibrosis and simply with gradual resolution of the edema and acute inflammation **(Matthay & Zemans, 2011).**

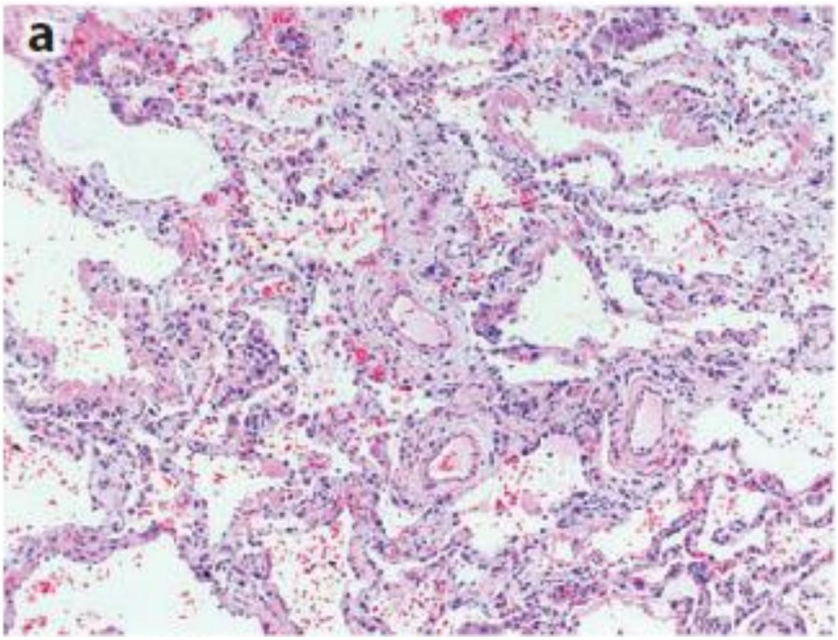
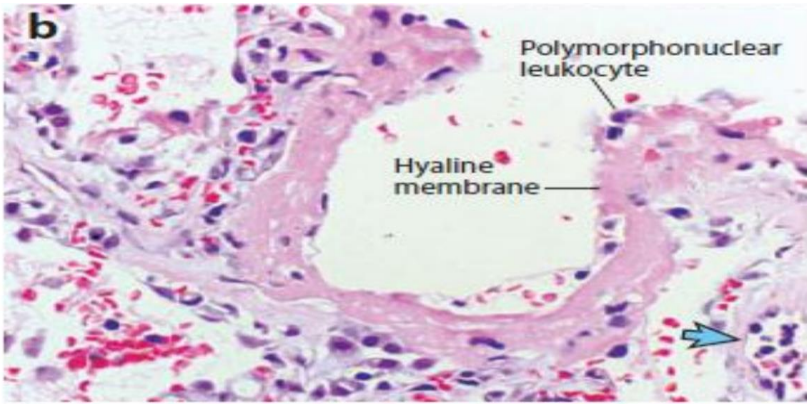
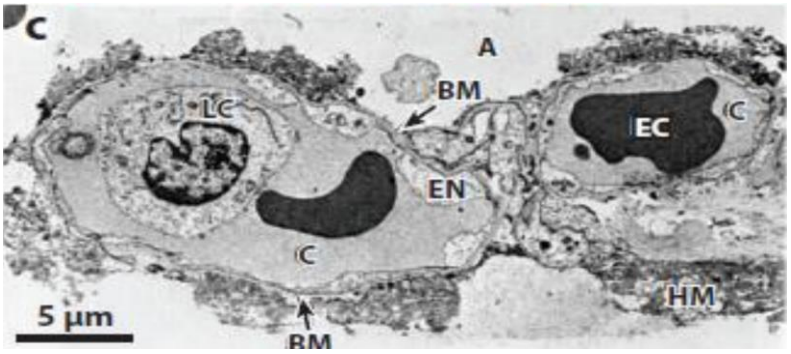


Figure (1): Histologic and ultrastructural analysis of the injured lung has been integral to current concepts of pathogenesis of acute lung injury/acute respiratory distress syndrome (ALI/ARDS).

(*a*) A low-power light micrograph of a lung biopsy specimen collected two days after the onset of ALI/ARDS secondary to gram-negative sepsis demonstrates key features of diffuse alveolar damage, including hyaline membranes, inflammation, intra-alveolar red cells and neutrophils, and thickening of the alveolar-capillary membrane.



(*b*) A higher-power view of a different field illustrates a dense hyaline membrane and diffuse alveolar inflammation. Polymorphonuclear leukocytes are imbedded in the proteinaceous hyaline membrane structure. The blue arrow points to the edge of an adjacent alveolus, which contains myeloid leukocytes.



(*c*) An electron micrograph from a classic analysis of ALI/ARDS showing injury to the capillary endothelium and the alveolar epithelium.

Abbreviations:

A, alveolar space; BM, exposed basement membrane, where the epithelium has been denuded; C, capillary; EC, erythrocyte; EN, blebbing of the capillary endothelium; LC, leukocyte (neutrophil) within the capillary lumen. The histologic sections in panels *a* and *b* are used courtesy of Dr. K. Jones, University of California, San Francisco. Reprinted with permission from the American Thoracic Society.