Acute respiratory distress syndrome: Epidemiology, pathophysiology, pathology, and etiology in adults

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INTRODUCTION

A distinct type of hypoxemic respiratory failure characterized by acute abnormality of both lungs was first recognized during the 1960s. Military clinicians working in surgical hospitals in Vietnam called it shock lung, while civilian clinicians referred to it as adult respiratory distress syndrome [1]. Subsequent recognition that individuals of any age could be afflicted led to the current term, acute respiratory distress syndrome (ARDS).

The epidemiology, pathophysiology, pathologic stages, and etiologies of ARDS will be reviewed here. Other issues related to ARDS are discussed separately. (See "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults" and "Acute respiratory distress syndrome: Prognosis and outcomes in adults" and "Acute respiratory distress syndrome: Ventilator management strategies for adults" and "Acute respiratory distress syndrome: Fluid management, pharmacotherapy, and supportive care in adults" and "Acute respiratory distress syndrome: Investigational or ineffective therapies in adults".)

EPIDEMIOLOGY

The incidence of acute lung injury was determined in a multicenter, population-based, prospective cohort study in the United States [2]. The study followed 1113 patients with ALI

(three quarters of whom had ARDS) for 15 months beginning in 1999 or 2000:

- The age-adjusted incidence was 86 per 100,000 person-years for individuals with an arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2) ratio ≤300 mmHg and 64 per 100,000 person-years for individuals with a PaO_2/FiO_2 ≤200 mmHg.
- The incidence increased with patient age from 16 per 100,000 person-years among individuals 15 to 19 years of age to 306 per 100,000 person-years among individuals 75 to 84 years of age.
- Extrapolation of the data suggested that there are approximately 190,000 cases of ARDS in the United States each year.

Within intensive care units, approximately 10 to 15 percent of admitted patients and up to 23 percent of mechanically ventilated patients meet criteria for ARDS [3-7]. As an example, in a multicenter, international study of nearly 30,000 intensive care unit (ICU) patients, 10 percent of admissions to the ICU were due to ARDS [7]. The majority of patients with ARDS (80 percent) required mechanical ventilation. Among those with ARDS, the majority (47 percent) had moderate ARDS while the remainder had mild (30 percent) or severe disease (23 percent). ARDS was responsible for 23 percent of patients mechanically ventilated in the ICU.

The incidence of ARDS varies geographically and may be higher in the United States and Europe than in other countries [7,8].

The incidence of ARDS may be decreasing. A prospective cohort study from a single institution reported that the incidence of ARDS decreased from 82.4 cases per 100,000 person-years in 2001 to 38.9 cases per 100,000 person-years in 2008 [9]. This was attributable to a decline in hospital-acquired ARDS, since the incidence of ARDS at hospital presentation did not change. Those who developed ARDS had more severe disease, more comorbidities, and more predisposing conditions. These findings may reflect changes in the delivery of care at this institution only; studies from other institutions are necessary before it can be concluded that the incidence of ARDS is declining in general.

PATHOPHYSIOLOGY

Healthy lungs regulate the movement of fluid to maintain a small amount of interstitial fluid and dry alveoli. This is interrupted by lung injury, causing excess fluid in both the interstitium and alveoli. Consequences include impaired gas exchange, decreased compliance, and increased pulmonary arterial pressure.

Baseline — Normal lung function requires that dry, patent alveoli be closely situated to appropriately perfused capillaries (picture 1) [10]. The normal pulmonary capillary endothelium is selectively permeable: fluid crosses the membranes under the control of hydrostatic and oncotic forces, while serum proteins remain intravascular.

The Starling equation describes the forces that direct fluid movement between the vessels and the interstitium [11]. A simplified version of the equation is:

$$Q = K \times [(Pmv - Ppmv) - rc\ (\pi mv - \pi pmv)]$$

where Q represents the net transvascular flow of fluid, K the permeability of the endothelial membrane, Pmv the hydrostatic pressure within the lumen of the microvessels, Ppmv the hydrostatic pressure in the perimicrovascular space, rc the reflection coefficient of the capillary barrier, πmv the oncotic pressure in the circulation, and πpmv the oncotic pressure in the perimicrovascular compartment. (See "Pathophysiology and etiology of edema in adults".)

The balance of hydrostatic and oncotic forces normally allows small quantities of fluid into the interstitium, but three mechanisms prevent alveolar edema (figure 1A-D) [11]:

- Retained intravascular protein maintains an oncotic gradient favoring reabsorption
- The interstitial lymphatics can return large quantities of fluid to the circulation
- Tight junctions between alveolar epithelial cells prevent leakage into the air spaces

Injury — ARDS is a consequence of an alveolar injury producing diffuse alveolar damage (picture 2 and picture 3) [12]. The injury causes release of pro-inflammatory cytokines such as tumor necrosis factor, interleukin (IL)-1, IL-6, and IL-8 [13-18]. These cytokines recruit neutrophils to the lungs, where they become activated and release toxic mediators (eg, reactive oxygen species and proteases) that damage the capillary endothelium and alveolar epithelium [12,19-23].

Damage to the capillary endothelium allows protein to escape from the vascular space. The oncotic gradient that favors resorption of fluid is lost and fluid pours into the interstitium, overwhelming the lymphatics [24]. The ability to upregulate alveolar fluid clearance may also be lost [25]. Increase in interstitial fluid, combined with damage to the alveolar epithelium, causes the air spaces to fill with bloody, proteinaceous edema fluid and debris from degenerating cells. In addition, functional surfactant is lost, resulting in alveolar collapse.

Consequences — Lung injury has numerous consequences including impairment of gas exchange, decreased lung compliance, and increased pulmonary arterial pressure.

- Impaired gas exchange – Impaired gas exchange in ARDS is primarily due to ventilation-perfusion mismatching: physiologic shunting causes hypoxemia, while increased physiologic dead space impairs carbon dioxide elimination [26,27]. A high minute volume is generally needed to maintain a normal arterial carbon dioxide tension ($PaCO_2$), although hypercapnia is uncommon. (See "Measures of oxygenation and mechanisms of hypoxemia".)

- Decreased lung compliance – Decreased pulmonary compliance is one of the hallmarks of ARDS [28]. It is a consequence of the stiffness of poorly or nonaerated lung, rather than the pressure-volume characteristics of residual functioning lung units [29]. Even small tidal volumes can exceed the lung's inspiratory capacity and cause a dramatic rise in airway pressures [28].

- Pulmonary hypertension – Pulmonary hypertension (PH) occurs in up to 25 percent of patients with ARDS who undergo mechanical ventilation [30-32]. Causes include hypoxic vasoconstriction, vascular compression by positive airway pressure, parenchymal destruction, airway collapse, hypercarbia, and pulmonary vasoconstrictors [33]. The clinical importance of PH in most patients with ARDS is uncertain. PH severe enough to induce cor pulmonale is rare, but it is associated with an increased risk of death [34,35].

PATHOLOGIC STAGES

ARDS tend to progress through three relatively discrete pathologic stages (the exudative stage, proliferative stage, and fibrotic stage), the details of which are discussed separately. (See "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults", section on 'Pathologic diagnosis and stages'.)

ETIOLOGIES AND PREDISPOSING FACTORS

ARDS has traditionally been conceptualized as a pattern of lung injury and clinical manifestations that can be caused by a variety of insults. However, the validity of the assumption that different inciting events cause a similar pattern of lung injury and similar clinical features has been questioned because numerous studies have found more severe reductions in lung compliance and less responsiveness to positive end-expiratory pressure (PEEP) when the ARDS was due to a pulmonary process than when it was due to an extrapulmonary precipitant, such as sepsis [36-39].

More than 60 possible causes of ARDS have been identified, and other potential causes continue to emerge as adverse pulmonary reactions to new therapies are observed (table 1). However, only a few common causes account for most cases of ARDS [6,40-43]. In one study of 107 patients in a medical intensive care unit, the most common etiologies were pneumonia (40 percent), sepsis (32 percent), and aspiration (9 percent) [44]. Factors that may predispose a patient to develop ARDS without causing ARDS directly have also been identified.

Sepsis — Sepsis is the most common cause of ARDS [40,41,45,46]. It should be the first etiology considered whenever ARDS develops in a patient who is predisposed to serious infection or in association with a new fever or hypotension. (See "Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis".)

The risk of developing ARDS may be particularly high among septic patients with a history of alcoholism [47-49]. This was illustrated by a prospective cohort study that determined the incidence of ARDS in 220 patients with septic shock [48]. The incidence of ARDS among patients who chronically use excess alcohol was 70 percent, compared with 31 percent among patients who did not chronically use excess alcohol. A possible explanation for these findings is that alcohol use disorder may decrease the concentration of glutathione in the epithelial lining fluid, predisposing the lung to oxidative injury [47,50,51]. Alternatively, chronic excess alcohol use may increase the risk of ARDS by enhancing inappropriate leukocyte adhesion to endothelial cells [52].

A secondary analysis from a multicenter observational cohort study investigated risk factors for the development of ARDS among septic patients presenting to the emergency department or admitted for high risk elective surgery [53]. Of the 2534 patients meeting criteria for sepsis, 156 (6.2 percent) developed ARDS. In a multivariable analysis, risk factors for ARDS included APACHE II score (OR 1.10, 95% CI 1.07–1.13), age (OR 0.97, 95% CI 0.96–0.98), shock (OR 2.57, 95% CI 1.62–4.08), pneumonia (OR 2.31, 95% CI 1.59–3.36), pancreatitis (OR 3.86, 95% CI 1.33–11.24), presence of acute abdomen (OR 3.77, 95% CI1.37–10.41), and quantity of fluid given during the first six hours in liters (OR 1.15, 95% CI 1.03–1.29). When stratified by the presence or absence of shock, total fluid infused was not associated with the development of ARDS in the group with shock (OR 1.05, 95% CI 0.87–1.28), whereas quantity of fluid was associated with ARDS among those without shock (OR 1.21, 95% CI 1.05–1.38). Only 9 percent of the cohort had shock, suggesting that further studies are needed to investigate the relationship between quantity of fluids given and the risk of developing ARDS among septic shock patients.

Aspiration — Observational evidence indicates that ARDS will develop in approximately one-third of hospitalized patients who have a recognized episode of aspiration of gastric contents [40,42,54].

It was initially suggested in a classic study by Mendelson that aspirated contents had to have a pH less than 2.5 to cause severe lung injury [55]; however, subsequent animal studies showed that aspiration of non-acidic gastric contents can also cause widespread damage to the lungs [56]. This suggests that gastric enzymes and small food particles also contribute to the lung injury.

The unexpected development of ARDS may be the only indication that an intubated patient has developed a tracheoesophageal fistula, which is a rare complication of intubation.

Pneumonia — Community-acquired pneumonia is probably the most common cause of ARDS that develops outside of the hospital [57]. Common pathogens include Streptococcus pneumoniae [58], Legionella pneumophila, Pneumocystis jirovecii (formerly called Pneumocystis carinii), Staphylococcus aureus, enteric gram-negative organisms, and a variety of respiratory viruses [59,60]. The local prevalence of select micro-organisms may also change the proportional likelihood of specific infectious etiologies (eg, high prevalence of SARS-CoV-2 during the COVID-19 pandemic and subsequent surges). (See "Epidemiology, pathogenesis, and microbiology of community-acquired pneumonia in adults" and "Clinical evaluation and diagnostic testing for community-acquired pneumonia in adults" and "COVID-19: Epidemiology, clinical features, and prognosis of the critically ill adult".)

Nosocomial pneumonias can also progress to ARDS. Staphylococcus aureus, Pseudomonas aeruginosa, and other enteric gram negative bacteria are the most commonly implicated pathogens. (See "Epidemiology, pathogenesis, microbiology, and diagnosis of hospital-acquired and ventilator-associated pneumonia in adults".)

Severe trauma — ARDS is a complication of severe trauma with approximately 10 percent developing ARDS following trauma [61]. There are several situations during which ARDS seems to be particularly common following trauma [62]:

- Bilateral lung contusion following blunt trauma [63].
- Fat embolism after long bone fractures. In this situation, ARDS typically appears 12 to 48 hours after the trauma. This complication has decreased since immobilization for transport to the hospital became routine [64]. (See "Fat embolism syndrome".)
- Sepsis may be the most common cause of ARDS that develops several days or more after severe trauma or burns.
- Massive traumatic tissue injury may directly precipitate or predispose a patient to ARDS [62,65].

A predictive model taking into account age, APACHE II score, Injury Severity Score (ISS), the presence of blunt traumatic injury, pulmonary contusion, massive transfusion, and flail chest injury has been shown to predict the development of ARDS among at-risk patients with severe trauma [66]. A report using data from the Trauma Quality Improvement Project database showed that the following risk factors were associated with the incidence of ARDS in trauma patients: older age, male sex, race (Black patients had a highest risk), use of steroids, lower Glasgow Coma Score (GCS), and higher ISS [67]. Other risk factors included chronic alcohol use, liver cirrhosis, bleeding disorders, diabetes, hypertension, congestive heart failure, previous myocardial infarction, stroke, smoking, lung disease, and peripheral vascular disease.

Although ARDS can contribute to the length of critical illness following severe trauma, it does not appear to independently increase the risk of death [68]. Trauma-related ARDS has a significantly better prognosis than ARDS that is not related to trauma [69]. Among trauma patients with ARDS, mortality is associated with increasing age, male sex, and lower-field GCS and higher ISS [67].

Massive transfusion — Transfusion of more than 15 units of red blood cells is a risk factor for the development of ARDS [41]. Because the need for massive transfusion identifies patients at high risk for ARDS from other causes, it may be difficult to determine the degree to which transfusions are independently responsible for lung injury [70]. Transfusion of smaller volumes of packed red blood cells may also increase the risk of developing ARDS, as well as increase the risk of mortality among patients with established ARDS [71]. (See "Massive blood transfusion".)

Transfusion-related acute lung injury — Transfusion of even one unit of a plasma-containing blood product sometimes causes ARDS [72,73]. Fresh frozen plasma, platelet, and packed red blood cell transfusions have all been implicated. By definition, respiratory distress becomes apparent within six hours of completion of the transfusion. The mechanism is incompletely understood and may be multifactorial. (See "Transfusion-related acute lung injury (TRALI)".)

Lung and hematopoietic stem cell transplantation — During the first two or three days after surgery, lung transplant recipients are prone to primary graft failure. This devastating form of ARDS is attributed to imperfect preservation of the transplanted lung. (See "Primary lung graft dysfunction".)

Hematopoietic stem cell transplant patients are at risk for ARDS due to a variety of infectious and noninfectious causes. Noninfectious insults include idiopathic pneumonia syndrome, engraftment syndrome, and diffuse alveolar hemorrhage [74]. The lung injury appears to be partly related to the inflammation associated with chemoradiation conditioning regimens, as well as T cell alloreactivity. (See "Pulmonary complications after allogeneic hematopoietic cell

transplantation: Causes" and "Pulmonary complications after autologous hematopoietic cell transplantation".)

Drugs and alcohol — ARDS can occur following an overdose. Drugs that have been implicated include aspirin, cocaine, opioids, phenothiazines, and tricyclic antidepressants [75,76]. Idiosyncratic reactions to other drugs (eg, protamine, nitrofurantoin), including certain chemotherapeutic agents, occasionally precipitate ARDS after therapeutic doses. Radiologic contrast media can also provoke ARDS in susceptible individuals [77]. Alcohol use disorder increases the risk of ARDS due to other causes (eg, sepsis, trauma) but does not cause ARDS [78,79].

Genetic determinants — It seems likely that there are genetic determinants that increase an individual's risk of developing ARDS, since only a small proportion of the patients who are exposed to typical insults actually develop ARDS [80]. Studies that link mutations in the surfactant protein B (SP-B) gene to an increased risk of ARDS support this notion [81,82]. Insertion-deletion polymorphisms associated with the angiotensin converting enzyme (ACE) gene have also been suggested as a possible risk factor for ARDS [83], although not all studies support this observation [84]. Mutations in the selectin P ligand gene (SELPLG) have also be proposed as susceptibility genes involved in the development of ARDS among individuals of European and African descent [85]. A genome-wide association study (GWAS) of patients of European decent with sepsis-induced ARDS reported a reduced association between the development of ARDS and the geners9508032 located within the Fms-related tyrosine kinase-1 (FLT1) gene which encodes vascular endothelial growth factor-1 (VEGF-1) [86].

Other risk factors — Other possible risk factors for ARDS include cigarette smoking [87,88], cardiopulmonary bypass [89,90], thoracic surgery [91], pneumonectomy [92], acute pancreatitis [93], obesity [94,95], blood type A (particularly the A1 subtype) [96,97], near drowning [54,98,99], and exposure to particulate matter with an aerodynamic <2.5 micrometers ($PM_{2.5}$) and ozone [100]. (See "Drowning (submersion injuries)".)

Venous air embolism can occasionally cause ARDS. Outside of the operating room, the most common portal of entry for the air is a central venous catheter left open to the air [101]. (See "Air embolism".)

LUNG INJURY PREDICTION SCORE

The lung injury prediction score (LIPS) identifies patients who are unlikely to develop ARDS. This was demonstrated by a prospective cohort study of 5584 patients, in which seven percent of the

cohort developed ARDS, resulting in a negative predictive value (ie, the percent of patients with a LIPS <4 who will not develop ARDS) of 97 percent [102]. A LIPS >4 predicted ARDS with a sensitivity and specificity of 69 and 78 percent, respectively. A smaller study, using a retrospective derivation and prospective validation cohorts reported similar results [103].

The LIPS is the sum of the points assigned for each of the following predisposing conditions: shock (2 points), aspiration (2 points), sepsis (1 point), pneumonia (1.5 points), orthopedic spine surgery (1.5 points), acute abdominal surgery (2 points), cardiac surgery (2.5 points), aortic vascular surgery (3.5 points), traumatic brain injury (2 points), smoke inhalation (2 points), near drowning (2 points), lung contusion (1.5 points), multiple fractures (1.5 points), alcohol abuse (1 point), obesity (BMI >30, 1 point), hypoalbuminemia (1 point), chemotherapy (1 point), fraction of inspired oxygen >0.35 or >4 L/min (2 points), tachypnea >30 breaths/min (1.5 points), oxyhemoglobin saturation <95 percent (1 point), acidosis (pH <7.35, 1.5 points), and diabetes mellitus (-1 point).

Future studies are likely to combine clinical risk factors and biomarkers to predict the development of ARDS. For example, one study showed that among patients with sepsis, serum levels of receptors for advanced glycation end products, angiopoietin-2, and chemokine (C-X-C motif) ligand 16 combined with the ratio of arterial oxygen tension to fraction of inspired oxygen predicted the development of ARDS [104].

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Acute respiratory distress syndrome (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Acute respiratory distress syndrome (ARDS) is a type of respiratory failure characterized by the acute onset of bilateral alveolar infiltrates and hypoxemia. The diagnostic criteria for ARDS are provided separately. (See "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults", section on 'Diagnosis'.)

- Approximately 10 to 15 percent of patients admitted to intensive care units have ARDS. The incidence of ARDS rises with age, ranging from 16 per 100,000 person-years among individuals 15 to 19 years of age to 306 per 100,000 person-years among individuals 75 to 84 years of age. (See 'Epidemiology' above.)

- Healthy lungs regulate the movement of fluid to maintain a small amount of interstitial fluid and dry alveoli. In patients with ARDS, this regulation is interrupted by lung injury, causing excess fluid in both the interstitium and alveoli. Consequences include impaired gas exchange, decreased compliance, and increased pulmonary arterial pressure. (See 'Pathophysiology' above.)

- Patients with ARDS tend to progress through three relatively discrete pathologic stages: the exudative stage, proliferative stage, and fibrotic stage. (See 'Pathologic stages' above and "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults", section on 'Pathologic diagnosis and stages'.)

- More than 60 possible causes of ARDS have been identified and other potential causes continue to emerge as adverse pulmonary reactions to new therapies are observed. However, only a few common causes account for most cases of ARDS; in the medical intensive care unit population, the most common causes include pneumonia, sepsis, and aspiration. Factors that may predispose a patient to develop ARDS have also been identified. (See 'Etiologies and predisposing factors' above.)

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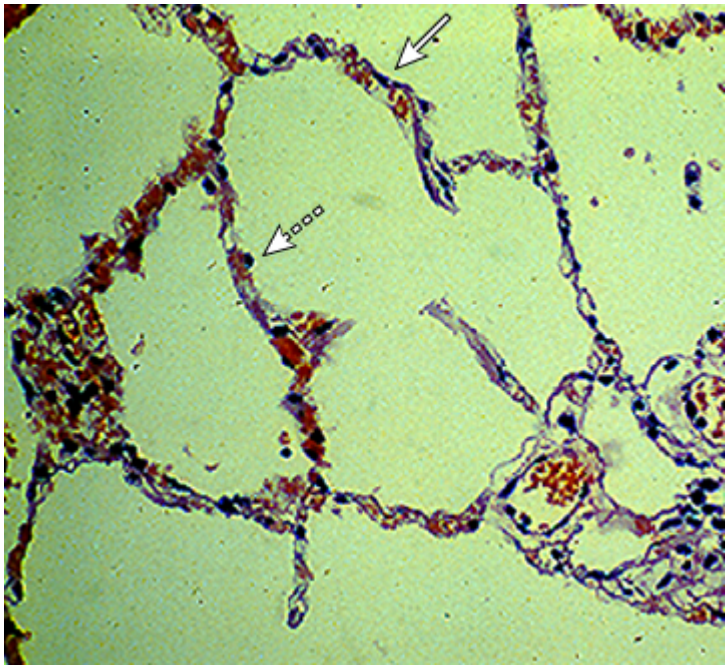
Topic 1609 Version 36.0

GRAPHICS

Normal lung

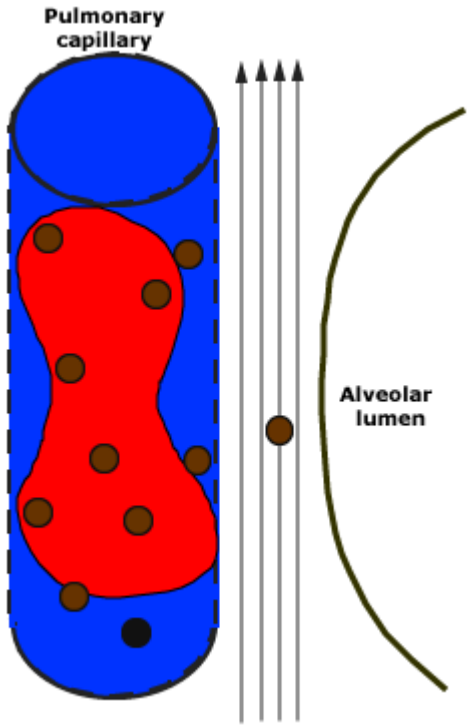


High-power photomicrograph shows alveoli containing capillaries within a narrow interstitium. The alveoli are lined with thin, elongated type I pneumocytes (arrow) and smaller numbers of cuboidal type II pneumocytes (dashed arrow).

Courtesy of Steven E Weinberger, MD.

Graphic 80140 Version 3.0

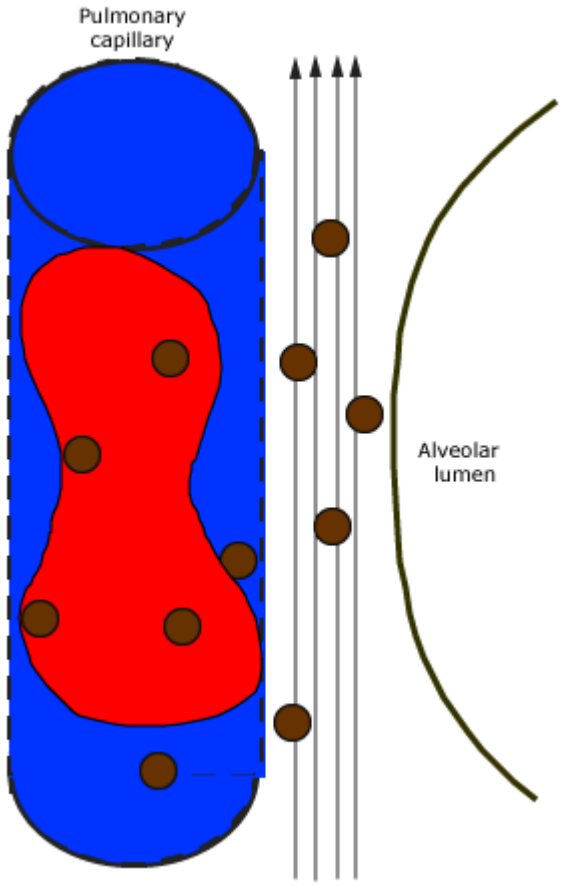
Protective mechanisms against pulmonary edema



An osmotic gradient favoring fluid reabsorption from the interstitium is maintained by retention of serum proteins within the intravascular space. Fluid which does leak into the interstitium is transported to lymphatics from which it is returned to the circulation. Finally, tight junctions between alveolar epithelial cells prevent leakage of fluid into the alveolar space. Arrows represent lymphatic movement; small circles represent protein.

Graphic 73684 Version 1.0

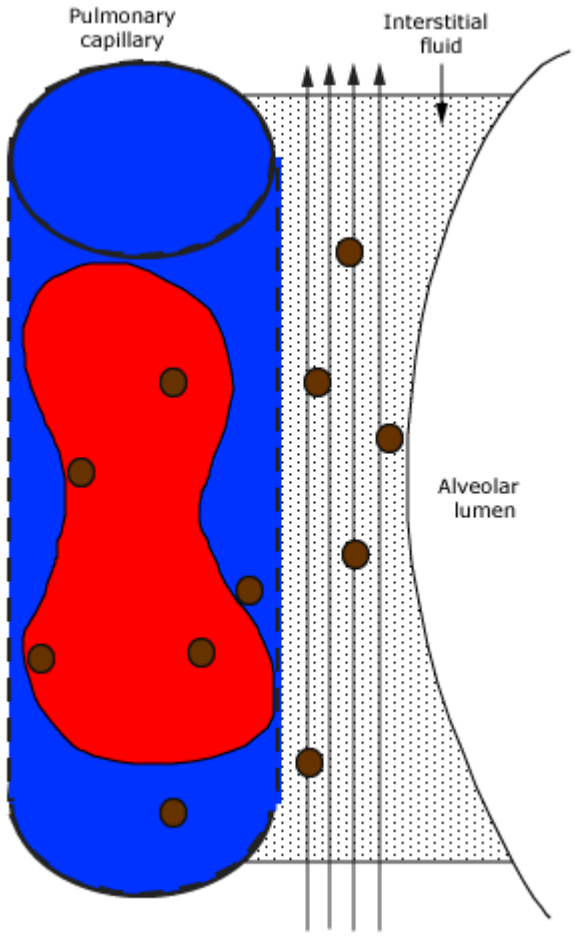
Early development of interstitial pulmonary edema



Breakdown of the capillary endothelial barrier allows leakage of serum proteins into the interstitial space, undoing the osmotic gradient which normally promotes fluid reabsorption. Arrows represent lymphatic movement; small circles represent protein.

Graphic 69933 Version 2.0

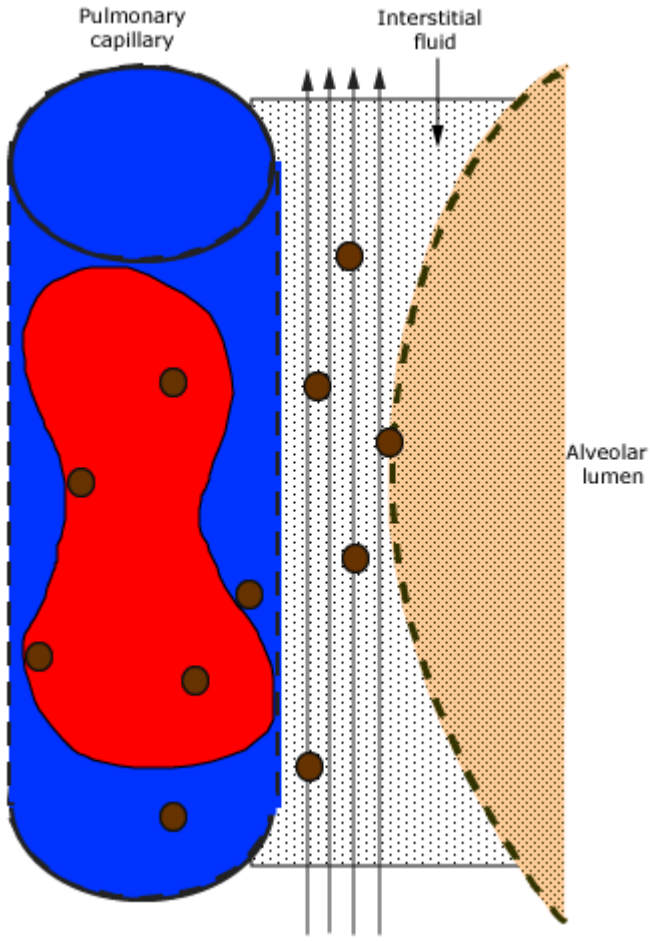
Late development of interstitial pulmonary edema



The quantity of fluid pouring from the capillaries overwhelms the capacity of the interstitium and the lymphatics, resulting in interstitial edema. Arrows represent lymphatic movement; small circles represent protein.

Graphic 73443 Version 2.0

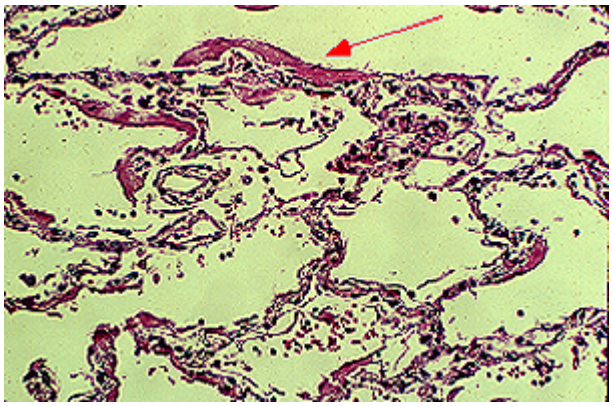
Development of alveolar edema



Breakdown of the alveolar epithelial barrier allows leakage of edema fluid into the alveolar space. Arrows represent lymphatic movement; small circles represent protein.

Graphic 61194 Version 1.0

Early diffuse alveolar damage

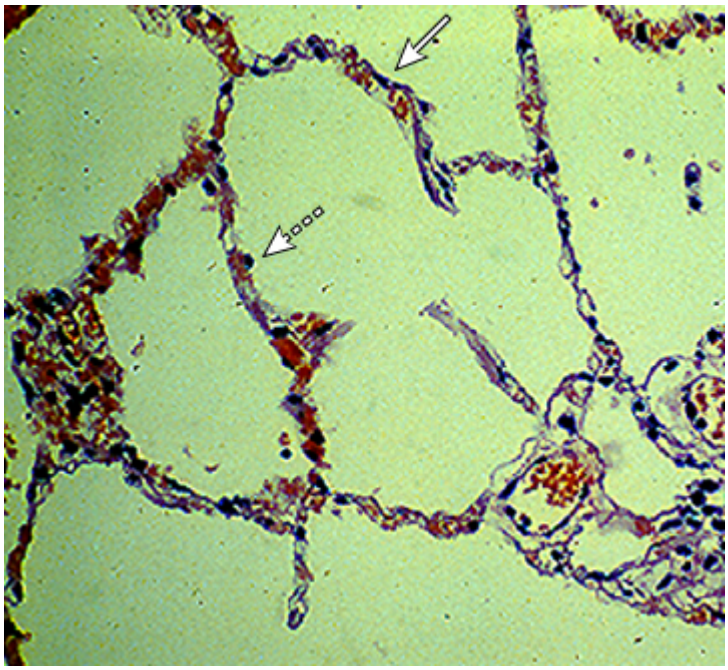


Photomicrograph shows early diffuse alveolar damage with minimal alveolar septal thickening, hyperplasia of pneumocytes, and eosinophilic hyaline membranes (arrow).

Courtesy of Jeffrey L Myers, MD.

Graphic 57964 Version 3.0

Normal lung

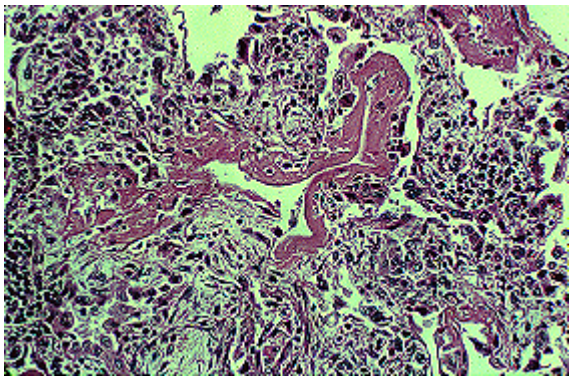


High-power photomicrograph shows alveoli containing capillaries within a narrow interstitium. The alveoli are lined with thin, elongated type I pneumocytes (arrow) and smaller numbers of cuboidal type II pneumocytes (dashed arrow).

Courtesy of Steven E Weinberger, MD.

Graphic 80140 Version 3.0

Late diffuse alveolar damage

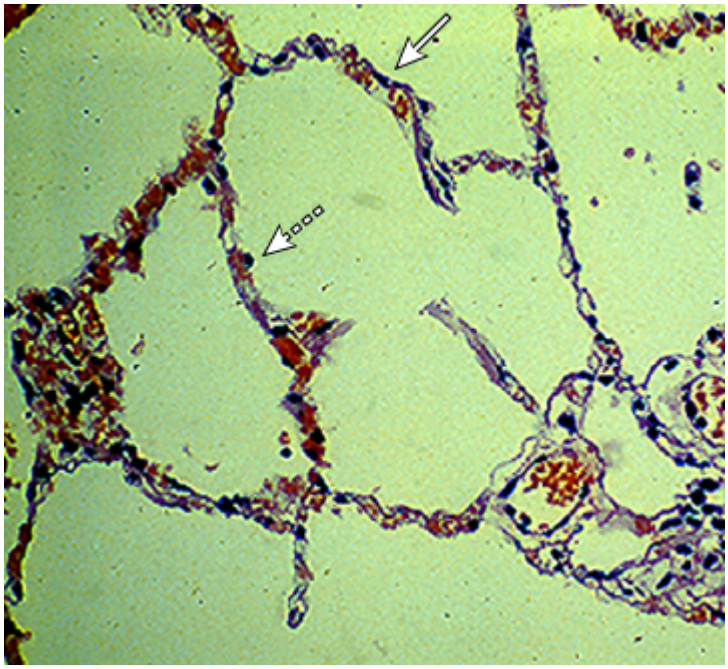


High power photomicrograph shows changes typical of the proliferative or late stage of diffuse alveolar damage. Although hyaline membranes are still identifiable, the histologic picture is now dominated by thickening and reorganization of interstitial structures due mainly to marked proliferation of mesenchymal spindle cells, including both fibroblasts and myofibroblasts.

Courtesy of Jeffrey L Myers, MD.

Graphic 65804 Version 3.0

Normal lung



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Courtesy of Steven E Weinberger, MD.

Graphic 80140 Version 3.0

Etiology of acute respiratory distress syndrome*

Etiology	Clinical features	Diagnostic tests
Sepsis	Fever, hypotension, leukocytosis, lactic acidosis, infectious source	Appropriate clinical context and positive cultures
Aspiration pneumonitis	Witnessed or risk for aspiration, food, lipid laden macrophages, airway erythema on bronchoscopy	Presumptive diagnosis with negative cultures
Infectious pneumonia (including mycobacterial, viral, fungal, parasitic)	Productive cough, pleuritic pain, fever, leukocytosis, lobar consolidation or bilateral infiltrates in an immunosuppressed patient	Appropriate clinical context and positive respiratory cultures
Severe trauma and/or multiple fractures	History of trauma or fractures within the last week	Diagnosis is apparent
Pulmonary contusion	History of chest trauma (blunt or penetrating), chest pain	Presumptive diagnosis in the correct clinical context, negative cultures
Burns and smoke inhalation	Exposure to fire or smoke, cough, dyspnea, DIC, particulate matter on bronchoscopy, surface burns	Presumptive diagnosis in the correct clinical context, negative cultures
Transfusion related acute lung injury and massive transfusions	History of transfusion, dyspnea during or shortly after transfusion	Diagnosis of exclusion
HSCT¶	History of HSCT	Diagnosis of exclusion
Pancreatitis	Abdominal pain, vomiting, risk factors (eg, gallstones, alcohol, viral infection)	Elevated amylase and lipase, with or without abnormal imaging
Inhalation injuries other than smoke (eg, near drowning, gases)	History of inhalation exposure (eg, chlorine gas)	Diagnosis of exclusion
Thoracic surgery (eg, post-cardiopulmonary bypass) or other major surgery	History of surgery, intraoperative ventilation, intraoperative transfusion	Diagnosis of exclusion
Drugs (chemotherapeutic agents, amiodarone, radiation)	New drugs or radiation exposure on history, lymphocytosis on lavage, lavage may have suggestive features of	Diagnosis of exclusion, lung biopsy occasionally helpful

	amiodarone toxicity ("foamy macrophages") but is nonspecific	

ARDS has over 60 etiologies. This is an abbreviated list of the common causes of ARDS.

AEP: acute eosinophilic pneumonia; ARDS: acute respiratory distress syndrome; COP: cryptogenic organizing pneumonia; DAD: diffuse alveolar damage; DIC: disseminated intravascular coagulation; HSCT: hematopoietic stem cell transplant.

* Use of the term ARDS to describe conditions such as AEP or COP is somewhat controversial. However, some experts consider these a "subtype" of ARDS since they present in a similar fashion to ARDS, although the pathology of such entities is different from DAD, which is the classic pathology associated with ARDS. Similarly, while neurogenic pulmonary edema meets the definition of ARDS since it causes hypoxemia and bilateral infiltrates in the absence of pulmonary edema due to heart failure, the pathology and clinical course is likely different. Similarly, embolism of fat, air, and amniotic fluid may mimic ARDS but it is uncertain as to whether they cause ARDS.

¶ Many patients with HSCT may develop a form of lung injury after transplant, but the distinction between this and ARDS due to complications of HSCT (eg, pneumonia) is often unclear.

Graphic 58759 Version 5.0