Ipsilateral pulmonary edema may occur in a lung that has been rapidly re-inflated after a period of collapse. The syndrome of re-expansion pulmonary edema is associated with variable degrees of hypotension and hypoxemia. In its extreme form, it may result in cardiac arrest and death. The initial cause of uninflated pulmonary parenchyma described with re-expansion pulmonary edema has typically been either a large undrained pleural effusion or a pneumothorax. The authors describe a patient in whom re-expansion pulmonary edema developed when inadvertent puncture of large emphysematous bullae released previously atelectatic lung.

(Key words: re-expansion pulmonary edema, giant bulla)

The first clinical description of a patient with re-expansion pulmonary edema (RPE) was published 90 years ago.1 This potentially fatal situation continues to be reported in the medical literature primarily as single case reports. Many physicians, therefore, remain unaware of the possibility of unilateral pulmonary edema following sudden re-expansion of previously atelectatic lung. The problem of high-permeability pulmonary edema after lung re-expansion is most frequently associated with elective thoracentesis or tube thoracostomy. Unexpected catastrophic pulmonary edema can also occur when large bullae are inadvertently ruptured and previously trapped lung parenchyma is suddenly decompressed. The occurrence of RPE may be reduced if the clinical predictors are recognized. This review emphasizes the clinical settings in which RPE is most likely to occur and examines the various physiologic explanations for this phenomenon.

Case report
A 50-year-old man presented after a 4-day history of progressive shortness of breath on exertion and finally at rest. He had had a transient mild pleuritic discomfort on his left side during a severe coughing episode 5 days earlier when exposed to a mixture of cleaning solvents at home. The coughing persisted for 1 day and was nonproductive. He denied fever, chills, or exposure to infectious disease, and had respiratory discomfort when lying supine or on his left side.

The patient had mild hypertension and admitted that he had been told recently that he had a “hole” in his left lung. He had a thirty-pack-year history of cigarette smoking and worked as an assembly line foreman for a manufacturing plant. He denied any significant occupational exposure.

Physical findings on admission included a slight shift of his trachea to the right, hyperresonance to percussion over the left hemithorax with diminished breath sounds, and distant normal heart sounds. Pulse was 82 beats/min, and blood pressure was 140/90 mm Hg. He was not cyanotic. He was tachypneic with 22 breaths/min, but was not uncomfortable in the seated position. The remainder of the physical examination was unremarkable.

Supplemental oxygen was provided by nasal cannula because the patient was dyspneic. Oxyhemoglobin saturation was 98% by pulse oximeter. Radiography of the chest revealed nearly complete left hyperlucency thought to be a pneumothorax (Figure 1). A 32 F chest tube was inserted, and a second radiograph was obtained to confirm tube position. This film failed to show re-inflation. When administration of continuous negative pressure to the left pleural space failed to expand the parenchyma, the patient underwent successful video-assisted thoracoscopic with surgical clipping.

Approximately 45 minutes after the successful re-expansion of the left lung, the patient became confused, cyanotic, and had respiratory distress. His pulse increased to 120 beats/min, while his blood pressure increased to 180/110 mm Hg. To maintain a PaO₂ of 60 torr, the patient required 60% oxygen and a positive end-expiratory pressure (PEEP) of 10 cm H₂O. The postprocedure radiograph confirmed the presence of left unilateral pulmonary edema (Figure 2). The patient gradually improved and was able to oxygenate without ventilator support on the fourth day.

Past images of the patient’s chest were retrieved from another hospital. Among these were chest radiographs similar to the one obtained at admission as well as a computed tomographic scan of the chest that confirmed the presence of a bulla that involved most of the left hemithorax (Figure 3).

Discussion
Re-expansion pulmonary edema is an uncommon acute lung injury that may follow rapid re-inflation of collapsed lung parenchyma. When the lung is suddenly re-expanded by large-volume thoracentesis or tube thoracostomy with applica-
ventilation. A high-permeability, intra-alveolar, perivascular edema that is usually confined to the hemithorax that contains the re-expanded lung may occur. The intra-alveolar flooding that results from increased capillary permeability creates an intrapulmonary shunt, as the re-expanded lung is now fully perfused while lacking effective ventilation.  

Typically, the patient with significant RPE becomes symptomatic within 15 minutes to 2 hours after the rapid re-expansion of the lung. Tachypnea and tachycardia are commonly associated with cyanosis. A cough that produces frothy pink sputum belies the presence of pulmonary edema, and end-inspiratory crackles are heard over the affected hemithorax. The patient’s dyspnea and hypoxemia fail to resolve with the administration of supplemental oxygen by mask or cannula. The resultant decrease in PaO2 may be severe enough to cause general tissue hypoxia, hypotension, and cardiac dysfunction and arrest. Radiographic opacities with an alveolar filling pattern become apparent within 2 to 4 hours after re-expansion, progress for 24 to 48 hours, and typically persist for 4 to 5 days if the patient survives.  

In retrospective studies of chest tube drainage of pneumothorax, the occurrence of RPE ranged from 1% to 14%. One of the predictors of re-expansion pulmonary edema is thought to be the duration of lung collapse. Human studies suggest that a lung that has been atelectatic for 3 or more days may develop edema with rapid re-expansion and reperfusion. Results of animal studies suggest a similar length of time, with incidence of RPE reaching 85% if the lung has been atelectatic for more than 8 days. Nevertheless, there are reports of re-expansion pulmonary edema occurring in situations when the documented duration of lung compression was brief, indicating that this is not the sole risk factor for edema development.  

The second suggested predictor is rapid re-expansion of the lung tissue, usually following the creation of relatively “excessive” negative pleural pressures by suction. The absolute level of negative pressure that has caused RPE has varied and may not be as critical as the rate of the re-expansion. Although emphasis is often placed on the amount of negative pleural pressure used during rapid re-expansion pulmonary edema, these forces do not have to exceed those commonly employed in clinical medicine. The occurrence of RPE after large-volume thoracentesis by gravity-dependent drainage supports this observation.  

Most investigators believe that the pathophysiology of RPE is multifactorial and involves mechanical and chemical stresses. During the time the lung is collapsed, some of the atelectatic parenchyma have regions in which alveolar gas is completely resorbed. Because the residual bronchial circulation does not supply the lung parenchyma, alveolar and vascular endothelial cells may be deprived of the oxygen required for continued metabolism of surfactant. Any absolute or relative abnormalities in this phospholipid augments the tendency of the collapsed lung to remain atelectatic by increasing inward lung recoil pressure.  

Additional biochemical changes occur during the period that the collapsed parenchyma is hypoxic. A decrease in mitochondrial oxygen use causes a shift to anaerobic metabolism. Under these conditions, investigators have documented an increase in two intracellular enzymes, xanthine oxidase and aldehyde oxidase, that are capable of promoting superoxide radical formation. Increased extramitochondrial release of pronated hydroperoxyl radicals may be promoted by decreased availability of mitochondrial dismutase in tissues undergoing sublethal ischemia. Thus, after a sufficient period of collapse and hypoxia, the capillaries deprived of oxygen have an increased release of endogenous free radicals that damage the vascular endothelium, resulting in leaky capillaries analogous to adult respiratory distress syndrome.  

The alveolar-capillary basement membrane of the lung is now in jeopardy of sustaining damage from the mechanical forces of rapid re-expansion superimposed on the biochemical changes associated with reperfusion/reoxygenation. The mechanism of vascular injury during re-expansion involves the linear stretching of the extra-alveolar vessels with increased tension on the alveolar septal walls. The torque on the relatively stiff parenchyma with decreased surfactant activity results in an increased transmural pressure gradient across the pulmonary microvessels that is augmented by the elevation of intravascular pressure as pulmonary artery flow resumes. This sudden imbalance of interstitial and hydrostatic forces favors a net transudation of fluid from the vasculature into
the interstitium. When the lymphatic system is overwhelmed, intra-alveolar flooding occurs and the intrapulmonary shunt is established. The ratio of alveolar fluid protein to serum protein concentration is greater than 0.7, indicating increased capillary permeability.18,19

In addition to mechanical forces, it is generally agreed that some of the alveolar-capillary injury occurs as a result of reperfusion in a manner consistent with hypoxia/reoxygenation injuries observed in other organs.22 In these situations, there is an enhanced reduction in mitochondrial respiratory chain components that results in superoxide production during reoxygenation.

The activation of the neutrophils in reperfused tissues may be triggered by the microvascular shearing and also contributes to free radical production.19 Analysis of the edema fluid will identify high concentrations of interleukin-8, LTB4, and P-selectin as well as the enzyme neutrophil elastase, suggesting a role for activated neutrophils.23

In addition to the proposed mechanisms of alveolar-capillary injury, there also seems to be an individual propensity for RPE, as not all patients respond to lung re-expansion in the same manner. In one study, incidence of RPE correlated with the age of the patient and occurred more frequently in patients aged 20 to 30 years than in patients over the age of 40 years. The authors speculated that age-related changes in the lung may provide some degree of protection against RPE.9

Treatment options are limited to maneuvers that decrease the newly created ipsilateral intrapulmonary shunt. Positioning the patient with the affected side up should allow better perfusion of the unaffected lung. Administration of misoprostil, a prostaglandin analogue, along with ibuprofen is untested, but has been recommended for cytoprotection and anti-inflammatory actions.24 The definitive intervention, however, is the application of PEEP with or without positive-pressure mechanical ventilation. This modality recruits alveolar surface area by increasing the functional residual capacity and displacing intra-alveolar water to change some alveolar units from shunts to areas of V/Q mismatch. Prompt intervention is critical for a good outcome, as approximately 20% of episodes of RPE are fatal.24,25

Re-expansion pulmonary edema is thought to be a result of combined alveolar-capillary membrane disruption and ischemia-reperfusion-mediated injury, initiated by stretching and distention and increased pulmonary flow that occur during pulmonary re-expansion. The condition is favored by previous atelectasis and rapid re-expansion of the lung parenchyma. This situation is clinically most common in treatment of pleural effusion and pneumothorax, but has occurred with removal of a large tumor26 and rupture of a giant bulla. Treatment is based on adequate oxygenation and circulation, typically with PEEP. Consideration and prevention of potential RPE when performing procedures is important, as mortality is consistently 15% to 20% despite mechanical ventilation.24
References


