

Reexpansion pulmonary edema

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ABSTRACT

Key points: (a) Reexpansion pulmonary edema - RxPE – is a rare form of acute lung injury, with an incidence of approximately 1% following evacuation of a pneumothorax; (b) RxPE usually follows rapid reinflation of collapsed lung parenchyma; (c) The most common factor associated with RxPE is the duration of lung collapse – more than 3 days seems to be the critical amount of time; (d) The pathophysiologic changes associated with RxPE are complex and not yet fully understood; (e) The pathologic process results from a combination of rapid pulmonary reexpansion with concurrent mechanical alveolar injury, decrease in surfactant and regional lung tissue hypoxemia, inflammatory cell migration and release of inflammatory mediators, and the resulting changes in capillary-alveolar barrier occurring concurrently with increased capillary/hydrostatic pressures; (f) Clinical manifestations of RxPE vary from minimal symptoms to life-threatening hypoxia and cardio-respiratory collapse; (g) The patient may experience dyspnea, thoracic pain, cough with or without pink/foamy sputum, cyanosis, rales and stertors on auscultation. Other clinical symptoms may include fever, nausea, vomiting, tachycardia, and hypotension; (h) The symptoms of RxPE usually appear within the first two hours following pulmonary reexpansion, but may be delayed by as many as 24 to 48 hours; (i) RxPE usually lasts clinically for as long as 1 to 2 days, but may take anywhere from 5 to 7 days to resolve; (j) Critical care practitioners should be familiar with the most common factors involved in the pathogenesis of RxPE; (k) The knowledge of these predisposing factors and the ability to effectively treat RxPE are important to prevention and treatment of this potentially fatal condition.

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INTRODUCTION

Reexpansion pulmonary edema (RxPE) is a rare form of acute lung injury. It usually follows rapid reinflation of collapsed lung parenchyma, with an incidence up to 1% following evacuation of a pneumothorax or a pleural effusion. Although RxPE was known as a clinical entity since at least the 1850's, its pathophysiologic mechanism remains to be fully elucidated. Because of the

associated significant mortality (as high as 21%), the most effective clinical approach to RxPE is prevention.

RxPE: RISK FACTORS

The phenomenon of RxPE is multifactorial. Pulmonary collapse lasting for over 72 hours is the single most important factor associated with the genesis of RxPE. Reexpansion pulmonary edema may also be related to: (a) the volume of the intra-thoracic space occupied by fluid, air, or a mass lesion; (b) clinical variables associated with pulmonary reexpansion technique or procedure – see below; (c) the presence of bronchial obstruction; (d) application of excessive suction to the tracheobronchial tree during bronchoscopy and/or suctioning with a tracheal suction catheter; (e) alteration of the pulmonary artery pressure; and (f) removal of large extrathoracic lesions (i.e., giant abdominal masses that exert compression on the thoracic cavity). Echevarria *et al* postulate that younger patient age may also be associated with greater propensity to develop RxPE.

It has also been suggested that one-lung ventilation during anesthesia may alter the distribution of blood flow between the non-dependent and dependent lungs, potentially predisposing to RxPE. In addition, Yanagitate *et al* speculate that thoracic epidural anesthetic administration may affect the sympathetic control of pulmonary circulation.

Of interest, a study of RxPE in a primate model by Miller *et al*, found that evacuating a large pneumothorax of three days duration using suction of $-10\text{ cm H}_2\text{O}$ versus *no suction* resulted in 100% incidence of RxPE in the *suction* group versus 0% incidence in the *no suction* group.

The amount of time the lung is collapsed (usually greater than 3 days)

Volume of the thoracic space occupied by the lesion (effusion/air/mass)

Removal of large extrathoracic lesions (i.e., giant abdominal mass)

Variables associated with the reexpansion technique/procedure

Presence of bronchial obstruction

Loss of surfactant (secondary to combination of other factors)

Alteration of pulmonary artery pressure

Application of excessive suctioning to the tracheobronchial tree

Patient age (younger patients may have greater predisposition)

Table 1. Summary of risk factors associated with RxPE. Modified from Genofre EH, Vargas SF, Teixeira LR, *et al*. Reexpansion pulmonary edema. J Pneumol 2003;29(2):101-106.

PATHOPHYSIOLOGY

The pathophysiology of RxPE is complex and involves several simultaneously occurring processes (**Figure 1**). Reexpansion pulmonary edema can be unilobar or multilobar, depending on the

degree of preexisting atelectasis. A study by Mahfood *et al*, described 93% of the cases being unilateral, with 6.7% being bilateral, and less than 1% being contralateral.

It has been proposed that rapid lung expansion following prolonged (3-7 days) pulmonary collapse contributes to increased pulmonary vascular permeability, loss of surfactant, and increased production of oxygen free radicals. When subjected to sudden re-expansion, the lung experiences simultaneous rapid increase in blood inflow and concurrent alveolar distention. This leads to increases in pulmonary capillary pressure, hydrostatic pressure, pressure-induced mechanical alveolar-capillary disruption, increased capillary permeability and transudation of fluid into the lung, **overflow of fluid and protein** contributing to the development of pulmonary edema, and finally hypoxia and hypoxic-induced cardiac dysfunction.

Simultaneously, increased blood flow and rapid alveolar distention lead to alterations in the alveolar-capillary barrier and alveolar injury secondary to the re-opening of atelectatic segments of the lung. Hydrostatic pressure elevations seen in RxPE are likely associated with elevations of various **selectin** proteins (**E-selectin**, **L-selectin** and **P-selectin**). This is then associated with the recruitment of neutrophils, release of neutrophil granular contents, and elevations in IL-8, MCP-1, nitric oxide, and free radical concentrations in the lung. These changes, in turn, exacerbate the imbalances in pulmonary fluid-protein homeostasis, leading to further worsening of pulmonary edema.

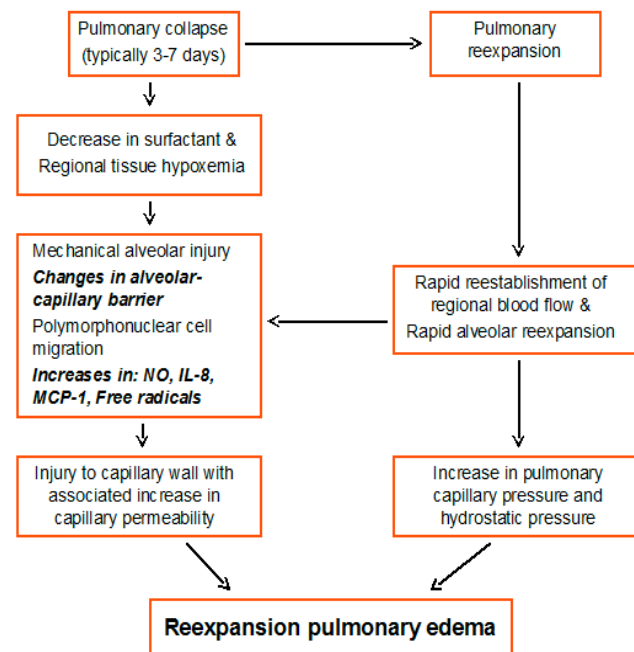


Figure 1. Proposed pathophysiologic mechanism of reexpansion pulmonary edema. Modified from Genofre EH, Vargas SF, Teixeira LR, *et al*. Reexpansion pulmonary edema. *J Pneumol* 2003;29(2):101-106.

DIAGNOSIS

The clinical diagnosis of RxPE is difficult. When making the diagnosis, it is important to carefully consider the clinical history, clinical presentation, and radiographic evidence. Clinical history often features prolonged nature (3-7 days) of the thoracic space-

occupying lesion and rapid removal of more than 1.5 liters of extrapulmonary thoracic contents (i.e., effusion, pneumothorax, mass). The symptoms of RxPE usually appear within the first two hours following pulmonary reexpansion, but may be delayed by 24 to 48 hours. Reexpansion pulmonary edema usually lasts clinically for as long as 1 to 2 days, but may take anywhere from 5 to 7 days to resolve.

The symptoms of RxPE vary from minimal or no symptoms (i.e., radiographic pulmonary edema only) to life-threatening hypoxia, hemodynamic instability, and death. The patient may experience dyspnea, thoracic pain, cough with or without pink/foamy sputum, cyanosis, rales and stertors on auscultation. Other clinical symptoms may involve fever, nausea, vomiting, tachycardia, and hypotension. The evolution of RxPE is highly variable, and often takes an unpredictable path, from spontaneous resolution to fatal respiratory failure.

Radiography will demonstrate pulmonary edema with interstitial opacities, pulmonary consolidations, air bronchograms, pulmonary clefts, and Kerley's "B" lines. Because of the variability in both clinical and radiologic features of RxPE, the differential diagnosis should include cardiogenic pulmonary edema, pulmonary infection, and pneumonitis.

TREATMENT

The treatment of RxPE consists of a combination of: (a) administration of supplemental oxygen; (b) ventilatory support (invasive versus non-invasive); (c) appropriate hemodynamic monitoring; (d) vasopressor and/or inotropic agent use; and (e) careful diuresis. Clinical maneuvers that may be helpful in the setting of RxPE include: (a) lateral decubitus position with the affected side facing up – this maneuver may reduce intrapulmonary shunting and improve oxygenation; (b) avoidance of application of excessive ventilatory pressures; and (c) occlusion of the pulmonary artery with a balloon catheter on the affected side – this maneuver is not routinely performed and should be used with extreme caution. In addition, negative pressure applied to the pleural space may need to be reduced or turned off (provided that any reductions in negative pressure would not lead to creation of intrathoracic tension physiology).

Several options may be entertained if the patient requires ventilatory support. Many patients do not exhibit significant increases in oxygen demand, and nasal cannula or face mask oxygen supplementation may be the only interventions needed. Some patients who do not need tracheal intubation benefit from CPAP or BiPAP delivered via specialized facial mask. In severe cases, patients may require tracheal intubation and application of positive end-expiratory pressure. In the setting of refractory pulmonary failure, differential two-lung ventilatory strategies have been described.

PREVENTION

Careful performance of pleural drainage procedures may be the key in preventing RxPE. It is crucial that the provider placing the pleural catheter is aware of the chronicity of the space-occupying pulmonary process. Over 80% of RxPE cases occur in patients with prolonged duration of lung collapse (3-7 days being the critical time frame).

It is also important to try to estimate the volume of the space-occupying process, which may be important when performing a

gradual, staged drainage. For example, in the setting of pre-existing pulmonary hypertension or severe hypoxemia, it is recommended that slow evacuation of the space-occupying process be performed under careful clinical monitoring conditions.

The proposed amount of intrathoracic volume that can be safely withdrawn varies from study to study. Most authors recommend that each drainage procedure or 'step' should not evacuate more than 1000 mL at a time, especially if the evolution of the space-occupying process took longer than 72 hours. Some have suggested that 1500 mL may represent a safe limit. A strategy of carefully monitoring the pleural pressure during thoracic drainage procedure has also been described, with larger volumes (up to 5000 mL) being able to be evacuated without the development of RxPE as long as the pleural pressures do not exceed -20 cm H₂O.

CONCLUSIONS

Over 80% of RxPE cases occur in patients with prolonged duration of lung collapse (3-7 days being the critical time frame). The etiology of reexpansion pulmonary edema is multifactorial. Because of potentially high mortality, the best clinical approach to RxPE is prevention. Careful performance of pleural drainage procedures may be the key in preventing RxPE. It is crucial that the provider placing the pleural catheter or surgically removing a mass lesion is aware of the chronicity of the space-occupying pulmonary process. If clinical signs of RxPE become apparent, prompt recognition and institution of supportive measures are important. Appropriate monitoring, hemodynamic support, and ventilatory assistance may be necessary.

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