NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-.

# Noncardiogenic Pulmonary Edema

**Authors**

Shane B. Clark; Michael P. Soos[1].

**Affiliations**

[1] McLaren Greater Lansing

Last Update: March 25, 2020.

## Introduction

Noncardiogenic pulmonary edema is a disease process that results in acute hypoxia secondary to a rapid deterioration in respiratory status. The disease process has multiple etiologies, all of which require prompt recognition and intervention. Increased capillary permeability and changes in pressure gradients within the pulmonary capillaries and vasculature are mechanisms for which noncardiogenic pulmonary edema occurs. To differentiate from cardiogenic pulmonary edema, pulmonary capillary wedge pressure is not elevated and remains less than 18 mmHg.[1][2] This is important to differentiate as the management changes based on this distinction. Other findings during the initial evaluation of the patient may include a lack of acute cardiac disease or inappropriate fluid balance, flat neck veins, and the absence of peripheral edema. Chest imaging may reveal a peripheral distribution of bilateral infiltrates with no evidence of excessive pulmonary vasculature congestion or cardiomegaly. An echocardiogram may also be used to confirm a lack of acute systolic or diastolic dysfunction. These findings suggest a noncardiogenic source. Arguably the most recognized form of noncardiogenic pulmonary edema is acute respiratory distress syndrome (ARDS), which is a noncardiogenic pulmonary edema that has an acute onset secondary to an underlying inflammatory process such as sepsis, pneumonia, gastric aspiration, blood transfusion, pancreatitis, multisystem trauma or trauma to the chest wall, or drug overdose.[3] Diagnosis of ARDS also requires bilateral infiltrates on chest radiograph with a ratio of the partial pressure of oxygen (PaO2) to the fraction of inspired oxygen (FiO2) to be less than 300 mmHg with positive end-expiratory pressure (PEEP) of 5 cmH2O. Clinical context also necessitates no evidence of acute heart failure or hypervolemia in the setting of ARDS. The scope of noncardiogenic pulmonary edema is much broader than ARDS. It includes other etiologies, which include high altitude pulmonary edema, neurogenic pulmonary edema, opioid overdose, salicylate toxicity, pulmonary embolism, reexpansion pulmonary edema, reperfusion pulmonary edema, and transfusion-related acute lung injury (TRALI). Treatment is specific to the underlying etiology, and all require prompt recognition as clinical decline can be rapid and severe.

## Etiology

Noncardiogenic pulmonary edema has a variety of etiologies that include[4][5]:

- Acute respiratory distress syndrome (ARDS)
- High altitude pulmonary edema (HAPE)
- Neurogenic pulmonary edema
- Opioid overdose
- Salicylate toxicity
- Pulmonary embolism
- Reexpansion pulmonary edema

- Reperfusion pulmonary edema
- Transfusion-related acute lung injury (TRALI)

## Epidemiology

Most of the different etiologies of noncardiogenic pulmonary edema are rare but are essential to include on broad differential diagnosis in the appropriate clinical setting. ARDS affects roughly 200000 patients in the United States, 75000 of which are associated with mortality. ARDS is also responsible for 10% of intensive care unit (ICU) admissions globally.[1] HAPE is a rare disease that does not have a systematic epidemiologic analysis; however, those who have risk factors for acute mountain sickness with assent to altitudes greater than 2250 meters are at risk for HAPE.[6] TRALI is the leading cause of death from a blood transfusion and is more commonly seen in critically ill patients, as these patients often require more transfused blood products, and can be found in 1 of 5000 units of packed red blood cells. TRALI also has increased incidence in blood products with a higher ratio of plasma content, with 1 in 2000 plasma containing components and 1 in 400 whole blood products. Female donors have a higher incidence of TRALI; this was thought to be due to human leukocyte antigen (HLA) antibiotics found in parous female donors.[7]

## Pathophysiology

The underlying pathology is at the microvascular level due to the increase in pulmonary vascular pressure. In addition to this, the capillaries also become leaky, causing the formation of edema. The imbalance between the hydrostatic and oncotic forces, along with the enhanced permeability of the pulmonary capillaries results in pulmonary edema.[8] The capillaries become permeable due to the underlying cause such as sepsis, pancreatitis, etc.

## History and Physical

History will include a patient who has had progressive worsening of respiratory status and increasing dyspnea. Depending on the specific etiology, this could happen very rapidly. A thorough evaluation should take place as disease processes such as ARDS can occur in the setting of an increased inflammatory response in the body, such as sepsis, trauma, pneumonia, and pancreatitis. History should also include medication review, specifically opioid and salicylate use, as these can rarely cause noncardiogenic pulmonary edema. Recent or current blood transfusions, risk factors for pulmonary embolism, recent thoracic surgery should be a consideration. With appropriate geography, rapid ascent with increasing altitude may cause noncardiogenic pulmonary edema, and this should warrant further inquiry if suspected. The physical examination can rule out a cardiogenic source of pulmonary edema. Flat neck veins, appropriate fluid balance, lack of peripheral edema are findings in noncardiogenic pulmonary edema.[9][10]

## Evaluation

The evaluation should exclude a cardiogenic source; this can be done by echocardiogram to assess any changes in left ventricular ejection fraction or acute changes in the systolic or diastolic function of the heart. If the etiology is unclear from physical examination or echocardiogram, definitive evaluation is possible by assessment of pulmonary capillary wedge pressure; wedge pressure of less than 18 mmHg will rule out a cardiogenic etiology. Chest imaging should be next, which, if ARDS is of concern, will show bilateral infiltrates. Arterial blood gas will reveal a PaO2/FiO2 ratio (P/F ratio) of less than 300 in ARDS.[11] Reexpansion and reperfusion pulmonary edema may cause unilateral pulmonary edema. TRALI should be considered in a patient with respiratory decline and hypoxia within 6 hours of a blood transfusion.[12]

## Treatment / Management

Treatment of noncardiogenic pulmonary edema involves addressing the underlying cause of the event. There are currently no treatment options to address the vascular permeability in ARDS. Therefore management involves supportive care and treatment of the underlying disease process until there is the resolution of the acute lung injury. Inhaled nitric oxide, prostacyclin, anti-inflammatory therapy, and high-frequency ventilation has not shown

consistent clinical benefit.[13] The other causes of noncardiogenic pulmonary edema are also managed similarly with supportive care, including supplemental oxygen or mechanical ventilation, if needed as well as addressing the inciting cause.

## Differential Diagnosis

Differential diagnosis should include cardiogenic pulmonary edema as this is a cause of pulmonary edema that needs to be ruled out. In the appropriate clinical context with systemic inflammation, sepsis, or severe injury, evaluation for ARDS is necessary. HAPE should be a diagnostic option if the history provides quick ascent in altitude. Medication and drug use should be reviewed to assess for salicylate toxicity and opioid overdose, as these often get overlooked as etiologies of pulmonary edema.[14][15] Pulmonary embolism should always be considered if presenting with dyspnea, tachycardia, or signs of hemodynamic instability. Reexpansion and reperfusion pulmonary edema should also be a differential, and the provider should consider TRALI if pulmonary edema and hypoxia present within 6 hours of a blood transfusion.[16] The following list of differentials should be reviewed:

- Acute respiratory distress syndrome (ARDS)
- Drug overdose from opioids and salicylates
- High altitude pulmonary edema (HAPE)
- Pulmonary embolism
- Transfusion-related acute lung injury (TRALI)

## Prognosis

Prognosis varies depending on the cause of noncardiogenic pulmonary edema. Severe ARDS carries a 40% mortality rate. HAPE recurs in 60% of patients who ascend above 4500 meters and have a previous diagnosis of HAPE.[17] Prognosis is poor in neurogenic pulmonary edema as this condition is associated with an insult to the central nervous system (CNS), 71% of those with intracranial hemorrhage were documented to have NPE. However, there are no statistics concerning NPE in the context of other neurologic conditions such as epilepsy.[18] Ischemia-reperfusion injury accounts for 25% of the mortality after lung transplantation.[19] Mortality from TRALI is 5 to 10%; however, it can reach 47% in critically ill patients.[20]

## Complications

The main complication from noncardiogenic pulmonary edema is ventilator-dependent respiratory failure requiring intubation and possible prolonged requirement of the ventilator, which necessitates prompt diagnosis to prevent the severity of this complication.[21]

## Deterrence and Patient Education

In appropriate situations, noncardiogenic pulmonary edema is preventable. Patients should be educated about HAPE if they have been found to have pulmonary edema in the setting of a rapid increase in altitude, as these patients risk a 60% chance of recurrence with a rapid ascent to greater than 4500 meters. Salicylate toxicity is a consideration in those with chronic use, and opioid users should receive education about the adverse effects of chronic opioid use and the possible sequela of pulmonary edema.[22]

## Enhancing Healthcare Team Outcomes

A collaborative healthcare team is vital to the prompt recognition of noncardiogenic pulmonary edema. The nursing staff is critical for the recognition of reactions during a blood transfusion, which, if acted on, can prevent TRALI. Pharmacists can have an active role in those being prescribed opioids and salicylates and can recognize the rare adverse effects of these drugs as the development of pulmonary edema. ARDS can more promptly be diagnosed in the

ICU with the care team cooperation between the intensive care physician, respiratory therapy, and nursing staff. Interprofessional communication at all levels plays a key role in case management and directing optimal outcomes. [Level V]

## Questions

To access free multiple choice questions on this topic, click here.

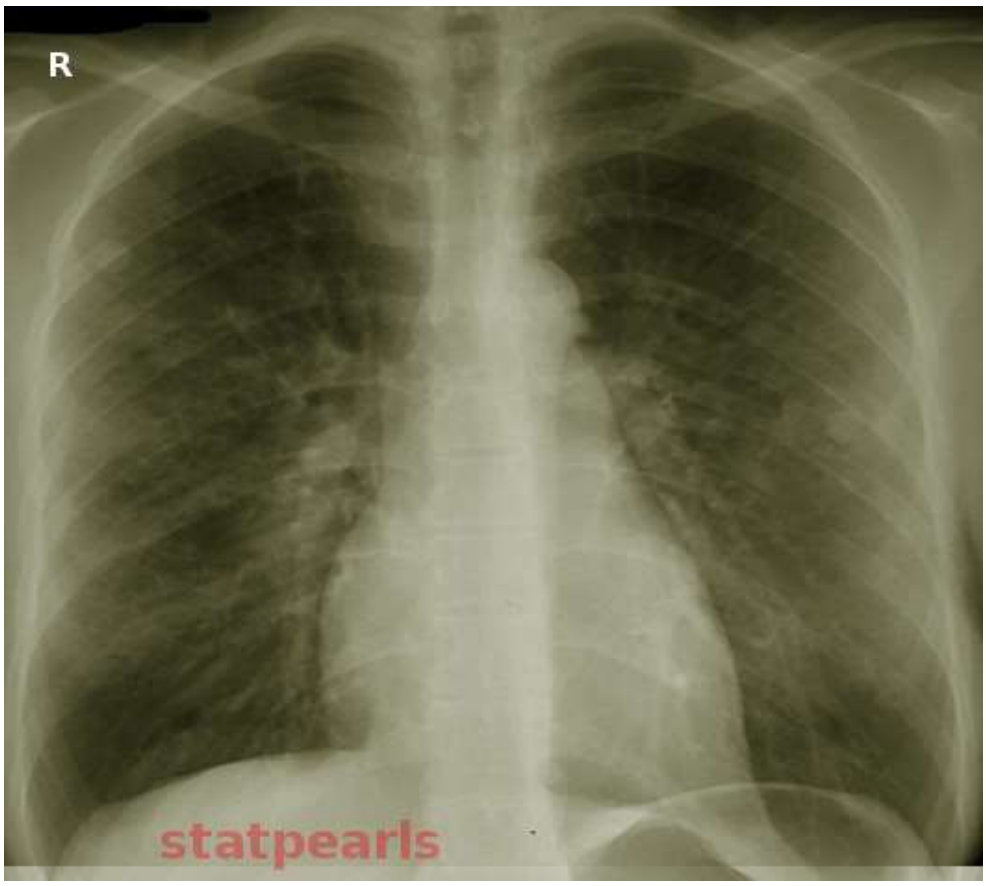
## References


1. Dries DJ. ARDS: From Syndrome to Disease: Prevention and Genomics. Air Med. J. 2019 Jan - Feb;38(1):7-9. [PubMed: 30711090]
2. Skalická H, Bělohlávek J. [Non-cardiogenic pulmonary edema, acute respiratory distress syndrome]. Cas. Lek. Cesk. 2015;154(6):273-9. [PubMed: 26750623]
3. Diamond M, Peniston Feliciano HL, Sanghavi D, Mahapatra S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jan 5, 2020. Acute Respiratory Distress Syndrome (ARDS) [PubMed: 28613773]
4. Patti R, Ponnusamy V, Somal N, Sinha A, Sharma S, Yoon TS, Kupfer Y. Naloxone-Induced Noncardiogenic Pulmonary Edema. Am J Ther. 2019 Nov 19; [PubMed: 31789629]
5. Clark SB, Soos MP. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 13, 2019. Noncardiogenic Pulmonary Edema. [PubMed: 31194387]
6. Luks AM, Swenson ER, Bärtsch P. Acute high-altitude sickness. Eur Respir Rev. 2017 Jan;26(143) [PubMed: 28143879]
7. Cho MS, Sharma S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jun 4, 2019. Transfusion-related Acute Lung Injury (TRALI) [PubMed: 29939623]
8. Suhail Najim M, Ali Mohammed Hammamy R, Sasi S. Neurogenic Pulmonary Edema Following a Seizure: A Case Report and Literature Review. Case Rep Neurol Med. 2019;2019:6867042. [PMC free article: PMC6803739] [PubMed: 31687236]
9. Akunov AC, Sartmyrzaeva MA, Maripov AM, Muratali Uulu K, Mamazhakypov AT, Sydykov AS, Sarybaev AS. High Altitude Pulmonary Edema in a Mining Worker With an Abnormal Rise in Pulmonary Artery Pressure in Response to Acute Hypoxia Without Prior History of High Altitude Pulmonary Edema. Wilderness Environ Med. 2017 Sep;28(3):234-238. [PubMed: 28673745]
10. Bachmann M, Waldrop JE. Noncardiogenic pulmonary edema. Compend Contin Educ Vet. 2012 Nov;34(11):E1. [PubMed: 23532787]
11. Mann A, Early GL. Acute respiratory distress syndrome. Mo Med. 2012 Sep-Oct;109(5):371-5. [PMC free article: PMC6179761] [PubMed: 23097941]
12. Fernandes Júnior CJ, Hidal JT, Barbas CS, Akamine N, Knobel E. Noncardiogenic pulmonary edema complicating diabetic ketoacidosis. Endocr Pract. 1996 Nov-Dec;2(6):379-81. [PubMed: 15251497]
13. Malhotra A, Drazen JM. High-frequency oscillatory ventilation on shaky ground. N. Engl. J. Med. 2013 Feb 28;368(9):863-5. [PMC free article: PMC4142426] [PubMed: 23339640]
14. Cohen DL, Post J, Ferroggiaro AA, Perrone J, Foster MH. Chronic salicylism resulting in noncardiogenic pulmonary edema requiring hemodialysis. Am. J. Kidney Dis. 2000 Sep;36(3):E20. [PubMed: 10977813]
15. Radke JB, Owen KP, Sutter ME, Ford JB, Albertson TE. The effects of opioids on the lung. Clin Rev Allergy Immunol. 2014 Feb;46(1):54-64. [PubMed: 23636734]
16. Tank S, Sputtek A, Kiefmann R. [Transfusion-related acute lung injury]. Anaesthesist. 2013 Apr;62(4):254-60. [PubMed: 23558721]
17. Korzeniewski K, Nitsch-Osuch A, Guzek A, Juszczak D. High altitude pulmonary edema in mountain climbers. Respir Physiol Neurobiol. 2015 Apr;209:33-8. [PubMed: 25291181]
18. Romero Osorio OM, Abaunza Camacho JF, Sandoval Briceño D, Lasalvia P, Narino Gonzalez D. Postictal neurogenic pulmonary edema: Case report and brief literature review. Epilepsy Behav Case Rep. 2018;9:49-50. [PMC free article: PMC5913356] [PubMed: 29692972]
19. Yabuki H, Watanabe T, Oishi H, Katahira M, Kanehira M, Okada Y. Muse Cells and Ischemia-Reperfusion Lung

Injury. Adv. Exp. Med. Biol. 2018;1103:293-303. [PubMed: 30484236]

20. Kim J, Na S. Transfusion-related acute lung injury; clinical perspectives. Korean J Anesthesiol. 2015 Apr;68(2):101-5. [PMC free article: PMC4384395] [PubMed: 25844126]
21. Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, Herridge M, Randolph AG, Calfee CS. Acute respiratory distress syndrome. Nat Rev Dis Primers. 2019 Mar 14;5(1):18. [PMC free article: PMC6709677] [PubMed: 30872586]
22. Sterrett C, Brownfield J, Korn CS, Hollinger M, Henderson SO. Patterns of presentation in heroin overdose resulting in pulmonary edema. Am J Emerg Med. 2003 Jan;21(1):32-4. [PubMed: 12563576]

## Figures




Non-cardiogenic pul edema. Image courtesy S Bhimji MD



Bookshelf ID: NBK542230 PMID: 31194387