

## Reversing Opiates in a Flash: Intranasal Naloxone-Induced Noncardiogenic Pulmonary Edema

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\* Discussant text in the article is expressed in italics.

**A** 27-year-old man with history of chronic neck pain and polysubstance abuse was found unresponsive with hypopnea at a party. Paramedics administered 3 sprays of intranasal naloxone (6mg) with improvement in mental status and respiratory effort.

*Naloxone is an opiate antagonist used to reverse the effects of opiate binding by mu receptors in the central nervous system. Indications for use include opiate-induced pruritus, rapid reversal of opiates after anesthesia, or overdose. Naloxone is available commercially in intravenous, intramuscular, subcutaneous, and intranasal forms. It is commonly used by first responders in the context of the national opiate epidemic. In many states, it is available without a prescription and is often prescribed to close contacts of individuals at risk of opiate overdose.<sup>1</sup>*

In transit to the emergency department, he became hypertensive and tachycardic. He developed hemoptysis and desaturation down to a SPO<sub>2</sub> of 40%. The patient was emergently intubated for respiratory failure.

*Classically, acute hypoxemic respiratory failure is severe arterial hypoxemia that is caused by intrapulmonary shunting of blood resulting from airspace filling or collapse.<sup>2</sup> Causes of hypoxemic respiratory failure include airspace filling secondary to elevated alveolar capillary hydrostatic pressure, as occurs in left ventricular failure or hypervolemia, increased alveolar capillary permeability, as occurs in*

*any of the conditions predisposing to acute respiratory distress syndrome (ARDS) blood (as occurs in diffuse alveolar hemorrhage) or inflammatory exudates (as occur in pneumonia or other inflammatory lung conditions)<sup>3</sup>. Patient's mental status puts patient at risk for aspiration pneumonia, but the patient's hemoptysis also makes diffuse alveolar hemorrhage or pulmonary embolism on the differential diagnosis. Chest X-ray would be a good initial diagnostic test.*

The patient was afebrile with BP of 168/92, heart rate of 108, and respiratory rate of 18 while saturating 95% on 100% FiO<sub>2</sub> with 8mmHg of PEEP. Physical exam revealed a well appearing man with endotracheal tube in place, sedated but arousable. Pupils were 4mm and reactive bilaterally. There was no jugular venous distension. Cardiac exam revealed tachycardic rate and regular rhythm without murmur. Lung exam revealed diffuse crackles in bilateral lung fields without wheezing. Abdomen was soft. Chest radiograph showed extensive airspace consolidations involving all lobes of both lungs without cardiomegaly. Laboratory studies were remarkable for leukocytosis to 14,200 and mixed respiratory failure with ABG of 7.33/58/37/29. Urine drug screen was positive only for oxycodone. Diuretic therapy was initiated in addition to ventilator support.

*The patient's chest radiograph showed bilateral infiltrates concerning for pulmonary edema. Pulmonary edema, either cardiogenic or non-cardiogenic, can be identified by diffuse*

*chest radiographic infiltrates that demonstrate a bilateral alveolar filling pattern. The distinction between the two types can be made on the presence of cardiomegaly, apical vascular redistribution, or Kerley "B" lines suggesting interstitial edema, which are typically features of cardiogenic edema. This patient had no evidence of heart failure.*

Bedside echocardiogram revealed normal heart function. Treatment with IV furosemide yielded rapid improvement. Chest radiographs on hospital day two revealed resolution of infiltrates. His respiratory status improved with subsequent extubation. The patient reported taking additional oxycodone prior to his respiratory event due to neck pain. A diagnosis of naloxone induced pulmonary edema was made.

*Previously published case series have identified a potential mechanism of action of naloxone induced pulmonary edema. Animal models suggest that rapid catecholamine surge results in acute neurogenic pulmonary hypertension. Systemic intravascular volume preferentially shunts to the low-pressure pulmonary vascular bed phenotypically producing acute respiratory distress syndrome (ARDS). Treatment includes respiratory support, diuresis, and pulmonary vascular vasodilation.<sup>3,4</sup>*

*Naloxone use is increasing in the setting of a national opiate epidemic. Often first responders make the decision to administer naloxone as in the case presented. However, internists should be aware of the po-*

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tential adverse reactions to naloxone, particularly when naloxone is administered in the field. In addition to pulmonary edema, internists should monitor for side effects including CNS disturbances such as seizure and hallucination; cardiac syndromes including arrhythmia and cardiac arrest; and pulmonary syndromes including pulmonary edema. Many of these side effects appear to be dose dependent. This case serves as a reminder for physicians to use naloxone in the smallest possible dose, to titrate to improvement in respiratory rate not mental status, and to monitor closely for side effects.

Note the following take home points:

1. Acute hypoxemic respiratory failure (AHRF) is caused by intrapulmonary shunting of blood resulting from airspace filling or collapse and typically presents with dyspnea and tachypnea.
2. Side effects of naloxone include pulmonary edema, seizures, hallucinations, arrhythmias, and cardiac arrest and may be dose-dependent.
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