Lesson 266: PreAnesthetic Assessment of the Patient With Negative Pressure Pulmonary Edema

WRITTEN BY:
Jonathan R. Ashton, MD
Staff Anesthesiologist, Memorial Hospital of Carbondale, Carbondale, Illinois

REVIEWED BY:
Suhail Istanbouly, MD
Attending Pulmonologist, Memorial Hospital of Carbondale, Carbondale, Illinois

DATE REVIEWED:
May 2007

DISCLOSURE STATEMENT
The author, reviewer, and editor have no relationships with pharmaceutical companies or manufacturers of products to disclose. This educational activity may contain discussion of published and/or investigational uses of agents for the treatment of disease. Some uses of these agents have not been approved by the FDA. Please refer to the official prescribing information for each product for approved indications, contraindications, and warnings.

NEEDS STATEMENT
Negative pressure pulmonary edema (NPPE) may develop suddenly, under many circumstances, and prove to be life-threatening for the patient. The anesthesiologist must be able to promptly recognize and treat the condition, given that the clinical presentation of several other disease processes requiring different therapies may mimic that of NPPE. This topic has been identified by committee as essential emergency information for practicing anesthesiologists.

TARGET AUDIENCE
Anesthesiologists

PREANESTHETIC ASSESSMENT

Dr. Elizabeth A.M. Frost, who is the editor of this continuing medical education series, is clinical professor of anesthesiology at The Mount Sinai School of Medicine in New York City. She is the author of Clinical Anesthesia in Neurosurgery (Butterworth-Heinemann, Boston) and numerous articles. Dr. Frost is past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is also editor of the book series based on this CME program, Preanesthetic Assessment, Volumes 1 through 3 (Birkhäuser, Boston) and 4 through 6 (McMahon Publishing, New York City).

A COURSE OF STUDY FOR AMA/PRA CATEGORY 1 CREDIT

Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before September 30, 2008. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours

RELEASE DATE: September 2007
TERMINATION DATE: September 30, 2008

ACREDITATION STATEMENT

The Mount Sinai School of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

LEARNING OBJECTIVES

At the end of this activity, the participant should be able to:
1. Review the incidence and association of laryngospasm and NPPE.
2. Describe the risk factors for NPPE.
3. List the means for preventing NPPE.
4. Discuss the signs and symptoms of NPPE and make a diagnosis.
5. Describe the appearance of NPPE on a chest X-ray film.
6. Recognize clinical scenarios that lead to NPPE.
7. Describe the effects of obstructed breathing on cardiac function.
8. Classify NPPE as noncardiogenic.
9. Explain the added effects of hypoxia and sympathetic stimulation in the development of pulmonary edema.
10. Prescribe a plan for the treatment of patients with NPPE.

CASE HISTORY

A 21-year-old African-American man was brought to the operating room for open reduction and internal fixation of his femur after he sustained a fracture when the golf cart he was driving overturned. His height was 6 ft and his weight about 300 lb. The patient was otherwise healthy and muscular, although he had been told that he snored and might benefit from sleep studies. On emergence from anesthesia, he appeared to be awakening appropriately and his trachea was extubated. Thereafter, ventilation became difficult and his oxygen saturation decreased.

CALL FOR WRITERS

If you would like to write a CME lesson for Anesthesiology News, please send an e-mail to Elizabeth A.M. Frost, MD, at ElzFrost@aol.com.

negative pressure pulmonary edema (NPPE) occurs in many clinical settings. This condition is of concern to anesthesiologists when it develops in a patient emerging from anesthesia as the consequence of an upper airway obstruction or laryngospasm. NPPE is the consequence of breathing through a partially or totally obstructed airway. Normal intrathoracic pressures become exaggerated, and circulatory hemodynamics are severely altered. Young, healthy, athletic, male patients are most prone to this complication because of their ability to generate high negative intrathoracic pressures. Such a connection was recognized by Holmes et al, who described the development of laryngospasm and pulmonary edema in 7 athletic adult patients immediately after extubation. As early as 1927, Moore and Binger had associated upper airway obstruction and pulmonary edema in spontaneously breathing dogs subjected to inspiratory resistance. Capitanio and Kirkpatrick recognized and described NPPE in children in 1973 after an examination of chest radiographs.
NPPE can develop from internal or external obstruction of the natural upper airway, which may occur in epiglottitis or strangulation. For example, Oswalt et al described 3 cases of acute pulmonary edema resulting from upper airway obstruction secondary to tumor mass, strangulation, and interrupted hanging.4 The patients recovered with treatment.

Other terms used to describe NPPE include negative pressure injury,2 postobstructive pulmonary edema I and II,6 athletic pulmonary edema,7 and postlaryngospasm pulmonary edema.8 NPPE is an important cause of perioperative morbidity and likely underreported. It can be mistakenly diagnosed in cases of pulmonary edema with other causes, such as fluid overload, myocardial infarction, and aspiration pneumonitis.

Epidemiology
Postanesthetic laryngospasm is among the most common causes of upper airway obstruction leading to pulmonary edema. The overall incidence of laryngospasm associated with general anesthesia is estimated to be 9 in 1,000 patients (0.9%) in the general population, and it is believed to be higher among patients undergoing otolaryngology procedures.8 NPPE follows laryngospasm in 5% to 10% of cases (Figure 1).

Tami et al reported pulmonary edema in 3 (11%) of 27 patients with acute upper airway obstruction.3 However, the investigators did not find any correlation with age, gender, history of cardiopulmonary disease, or fluid administration. Deepika et al reported 30 cases of NPPE during a 4-year period, for an incidence of 0.094%; patients undergoing head and neck surgery were found to be at higher risk.3 An overall incidence of NPPE of less than 0.1% was found in patients who have an obstructed airway after the generation of high negative intrathoracic pressure when they attempt to breathe; the culmination of this process is pulmonary interstitial and alveolar edema. Signs and symptoms of an obstructed airway and pulmonary edema include the following: intercostal and substernal retractions, the use of accessory muscles of breathing, rales, rhonchi, wheezing, the presence of pink frothy secretions in the airway, tachypnea, hypoxia, cyanosis, shortness of breath, agitation, and panic. The presence of pink frothy secretions in the airway is described as the hallmark of NPPE. Inspiratory "crowing" may be heard (Figure 2).

NPPE should be suspected based on findings of bilateral, centralised pulmonary edema on chest X-ray images and a normal cardiothoracic ratio in the immediate postoperative period (Figure 3).4 A heart size on chest X-ray images that is less than half of the total lung size is considered normal.10 The region of distribution of pulmonary edema helps differentiate cardiogenic from noncardiogenic causes. Noncardiogenic NPPE is similar to the edema seen in patients with ARDS, which usually develops as a result of increased capillary permeability and has a peripheral distribution. However, on chest X-ray images, NPPE resembles cardiogenic pulmonary edema, displaying a more central and perihilar distribution (likely caused by significant transient cardiac stresses).

Signs on chest X-ray images of pulmonary edema caused by increased capillary hydrostatic pressure (as occurs in NPPE) may include sepal lines, widened vascular pedicles, pleural effusions, peribronchial cuffing, and increased cardiac size. The predominant initial radiographic pattern resulting from increased hydrostatic pressure is interstitial edema, which is followed by alveolar edema. Signs on chest X-ray images of increased capillary permeability edema include a patchy and peripheral distribution, alveolar filling, and a normal heart size. However, the identification of sepal lines and pleural effusions is rare. Forster and colleagues suggested that the pattern of centralised edema resulting from increased hydrostatic pressure may be due to a gradient of interstitial fluid pressure from the peripheral interstitial connective tissue around smaller blood vessels to the more centralised, larger hilar vessels.12 Most patients with NPPE have features of both interstitial edema (including ground glass opacity and Kerley lines, which are thin, linear pulmonary opacities associated with the infiltration of fluid or cells into the pulmonary interstitium) and alveolar edema appearing with air space

Table 1. Pediatric Cases of Pulmonary Edema After Upper Airway Obstruction13

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>Patients in Whom Pulmonary Edema Developed, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute obstruction</td>
<td>167</td>
</tr>
<tr>
<td>Acute obstruction with chronic disease</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
</tr>
</tbody>
</table>

1. Pink, frothy secretions
2. Intercostal and substernal retractions
3. Rales, rhonchi, wheezing
4. Tachypnea
5. Decreased SpO2
6. Cyanosis

Figure 2. Signs of airway obstruction and pulmonary edema.
consolidation. A ratio of protein concentration in the pulmonary edema fluid to that in plasma of less than 0.65 is characteristic of pulmonary edema caused by increased hydrostatic pressure. This mechanism is believed to play a larger role in NPPE than in pulmonary edema caused by increased capillary permeability, in which the protein ratio is generally between 0.75 and 1.0. The pulmonary edema on chest X-ray images obtained in the latter scenario may be symmetric, asymmetric, or unilateral.

Electrocardiography in patients with NPPE reveals sinus tachycardia; echocardiography generally reveals normal valves and contraction. Blood pressure is often initially high in patients with NPPE. Serial measurements of troponin and creatinine phosphokinase levels, along with echocardiography, are used to exclude a diagnosis of myocardial damage. The blood level of brain natriuretic peptide—which may help to differentiate pulmonary edema from congestive heart failure—is generally normal.

An alteration in the permeability of alveolar capillary membranes is the accepted mechanism in ARDS. The multiple causes of ARDS include shock, sepsis, and aspiration. Pulmonary edema, which has also been associated with overdosing of opioids, may be caused by increased capillary permeability induced by hypoxia. The neurogenic pulmonary edema associated with elevated intracranial pressure may be caused by both elevated intravascular pressure and pulmonary capillary leakage, related to a release of catecholamine from the injured brain. Mortality is high. Exaggerated intrathoracic negative pressures leading to NPPE may be a result of rapid decompression of a pneumothorax resulting from excessive suction—referred to as re-expansion pulmonary edema (RPE). Unilateral pulmonary edema is seen on chest X-ray images.

Pulmonary edema with other causes, such as fluid overload and cardiac problems, which requires different management, should be ruled out. Differentiation should be possible by reviewing the patient’s history for any preexisting myocardial dysfunction and conducting a physical examination.

Clinical Presentation

Pulmonary edema associated with acute inflammation and upper airway obstruction (eg, epiglottitis, croup) is unusual but does occur. Travis et al reported the case of a 2.5-year-old child admitted to the hospital with fever, coughing, shortness of breath, inspiratory stridor, and cyanosis who exhibited intercostal and sternal retractions and a tracheal tug. The trachea was intubated and copious pink frothy secretions were suctioned. In a second case, a 9-year-old girl with croup was admitted with hoarseness, irritability, and suprasternal and intercostal retractions. The aryepiglottic folds were noted to be erythematous on intubation, and pink frothy fluid was found in the airway.

Biting on an inserted endotracheal tube or supraglottic airway device is a frequent cause of NPPE. Petrou and colleagues reported the case of a young man in whom NPPE developed after a vasectomy. He bit on the supraglottic airway device and, in the absence of a bite block, occluded the lumen. Strenuous inspiratory efforts cause excessive negative intrathoracic pressures. Laryngospasm, in addition to an obstructed natural or artificial airway, is an associated factor. Devys et al described a patient who bit on the laryngeal mask while breathing spontaneously during recovery. Five minutes later, dyspnea and mild hemoptysis developed. An examination of the patient’s airway revealed no abnormalities or injury. The electrocardiogram and cardiac enzyme levels were normal.

Possible problems associated with use of a supraglottic airway include poor positioning, airway obstruction from laryngospasm, and biting the tube. The intentional clenching of teeth can generate an occlusion force of 150 psi. Laryngospasm develops in 1% to 3% of cases when a laryngeal mask airway is placed—most commonly during induction of and emergence from anesthesia. In his seminal paper, Brain recommended the placement of a bite block until the patient recovers from anesthesia whenever a laryngeal mask airway is used.

Reversible cor pulmonale may develop in children with chronic upper airway obstruction caused by hypertrophic tonsils and adenoids. Hypoxia and hypercapnia associated
with chronic upper airway obstruction may cause pulmonary hypertension and subsequent cor pulmonale. Despite the frequency of laryngospasm in children, postobstructive pulmonary edema is rare. The extremely compliant chest wall in children may protect them against the increased negative pleural pressure associated with upper airway obstruction.

Taha et al described the case of a 3-year-old child with cerebral palsy in whom upper airway obstruction secondary to laryngospasm developed after extubation. The child was reintubated and pink frothy fluid was suctioned. Muscle spasticity and slow recovery from inhalational anesthesia are reported to be associated with cerebral palsy. The brain damage in cerebral palsy affects descending inhibitory neurons; the result is an inadequate release of gamma-aminobutyric acid, a principal inhibitory neurotransmitter, and a relative excess of excitatory transmitters such as glutamate. Thus, an association may exist between muscle spasticity, unpredictable recovery from anesthesia, and the development of NPPE.

In human volunteers, obstructive periods as short as 10 to 30 seconds have precipitated pulmonary edema. Ranta et al reported a case in which NPPE developed in a patient who had choked on a piece of chicken. Bronchoscopy and esophagoscopy findings were negative except for the presence of pink frothy secretions. Therapy involved mechanical ventilation with PEEP while the patient was in the prone position; it was anticipated that gravitational positioning would result in the redistribution and reabsorption of fluid in the lungs, as well as an improvement in the ventilation to the injured or atelecstatic lung.

Sullivan reported a case in which unilateral pulmonary edema followed the development of laryngospasm while a patient was in the lateral position. A laryngeal mask airway device had been used. A chest X-ray image showed edema of the dependent lung, believed to be due to increased blood volume and hydrostatic pressure. Unilateral pulmonary edema has developed following post-extubation laryngospasm in a patient in the right lateral recovery position. Contralateral NPPE has occurred after the administration of an interscalene block. This block is commonly accompanied by paralysis of the phrenic nerve, and diaphragmatic weakness may have limited an increase in negative pressure on the blocked side of the chest. Other cases of NPPE have been described in various clinical situations (Table 2). Frank pulmonary hemorrhage associated with NPPE is rare. The classic description of NPPE includes the appearance of serosanguineous or pink frothy fluid that may imply failure of the alveolar–capillary membrane, causing alveolar edema and some degree of bleeding. In a rabbit model, the alveolar–capillary membrane failed at a hydrostatic pressure in the microvasculature of approximately 40 mm Hg.

Airway bleeding is not an uncommon feature of NPPE. Bhavani-Shankar and colleagues suggested that NPPE should be renamed negative pressure injury to reflect the pathophysiology. The rapid development of large, subatmospheric pressures, as can occur in a lung capillary laryngospasm, may disrupt the tracheobronchial vasculature and cause airway bleeding. cigarette smoking and bronchitis have been reported to increase the friability of the vascular mucosa and increase susceptibility to negative pressure injury. Bronchoscopic findings in patients with NPPE may include diffuse hemorrhages in the tracheal and bronchial mucosa, possibly caused by the rupture of bronchial vessels, which contribute to the pinkish color of the secretions.

**Etiology**

During the periorperative period, the most common cause of acute obstruction in the upper airway leading to pulmonary edema is premature extubation with subsequent airway obstruction and/or laryngospasm. Laryngospasm is described as an involuntary contraction of the adductor muscles, primarily the lateral cricoarytenoid and possibly the thyroarytenoid, which control the vocal cords. This reflex is intended to protect the airway from water, secretions, and foreign material. NPPE is most frequently seen in young, healthy, athletic men who have well-developed thoracic musculature enabling them to generate high negative intrathoracic pressures. NPPE has at times been referred to as athletic pulmonary edema.

Only a few cases of NPPE have been reported in elderly patients, which suggests that an aging physiology may protect them from this complication. Elderly persons may have a weaker thoracic musculature and thus lack the ability to generate excessive negative pressure, or the permeability of the alveolar capillary membranes may be decreased. Pathologic studies of lungs from patients older than 60 years demonstrated thickening of the alveolar septa, and the term “senile lung” has been applied.

Other patients at risk for NPPE include those with obstructive sleep apnea and chronic obstruction of the upper airway. The physical profile of such patients includes obesity, short stature, stocky or muscular neck, and abnormalities of the nasopharyngeal soft tissue, including the presence of benign or malignant masses. Patients with thyroid masses or acromegaly, who also have an enlarged tongue, soft-tissue hypertrophy, and mandibular prognathism, are also at risk.

Multiple physiologic events result in primarily increased capillary hydrostatic pressure, in addition to some degree of increased capillary permeability edema (Figure 4). Negative intrathoracic pressure and hypoxia lead to pulmonary edema. Inspiration normally increases venous return to the heart. An intrapleural pressure of about –5 cm H2O is produced by lung elasticity, which results from a high content of elastin fibers and surface tension. The lung thus has a tendency to collapse against the resistance of the less mobile costochondral skeletal rib cage and its tendency to expand.

Lymphatic drainage of the normal physiologic transudate between the visceral and parietal layers of the pleura maintains the negative pleural pressure. The normal transpulmonary pressure is 5 cm H2O (4 mm Hg) and is measured by subtracting the intrapleural pressure from the alveolar pressure. Alveolar pressure is normally atmospheric at end-inspiration and end-expiration when there is no airflow. During inspiration, the intrapleural pressure decreases from –5 to –7.5 cm H2O, allowing atmospheric air to flow into the lungs. During expiration, diaphragmatic relaxation returns the intrapleural pressure to –5 cm H2O, and the elastic recoil of the lungs causes air to flow out of the alveoli.

Starling’s equation for fluid hemodynamics states that it is the balance or difference between hydrostatic and colloid osmotic pressures on each side of a semipermeable membrane (such as the lung capillary endothelium) that determines fluid flux and the development of pulmonary edema. Normal forces tending to move fluid outward from the capillaries into the pulmonary interstitium include 7 mm Hg of hydrostatic capillary pressure, 14 mm Hg of interstitial fluid colloid osmotic pressure, and 8 mm Hg of negative interstitial fluid pressure, for a total outward force of 29 mm Hg. The force tending to cause movement of fluid into the capillaries is 28 mm Hg of plasma colloid osmotic pressure. The net mean filtration pressure is 1 mm Hg of outward flow of fluid from the capillaries into the interstitial space, which allows nutrients to reach the tissues (Figure 5).

The average capillary hydrostatic pressure is determined by both arterial and venous pressures. An increase in either arterial or venous pressure increases capillary hydrostatic
The normal increase in venous and inspiratory resistance This pres- pulsus paradoxus

In Pulmonary edema

Pulmonary edema

Pulmonary edema

Figure 4. Mechanisms by which pulmonary edema may develop.

<table>
<thead>
<tr>
<th>Outward force</th>
<th>Hydrostatic capillary pressure, 7 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Interstitial fluid colloid osmotic pressure, 14 mm Hg</td>
</tr>
<tr>
<td></td>
<td>Negative interstitial fluid pressure, 8 mm Hg</td>
</tr>
<tr>
<td></td>
<td>Total, 29 mm Hg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inward force</th>
<th>Plasma colloid osmotic pressure, 29 mm Hg</th>
</tr>
</thead>
</table>

| Net          | 1 mm Hg outward force |

Figure 5. Forces of fluid movement in pulmonary capillaries.

pressure; however, a change in arterial pressure has only one fifth the effect of a change in venous pressure. Venous resistance is low, and a change in venous pressure is readily transmitted back to the capillaries. Arterial resistance is high, and a change in arterial pressure is minimally transmitted downstream.57

Albumin generates about 70% of normal oncotic pressure. The oncotic pressure increases along the length of the capillaries, particularly in capillaries having a high net filtration rate, because the unfiltered capillary fluid has higher concentration of protein. Although the oncotic pressure is only about 0.5% of the total osmotic pressure, it is important because colloids do not cross capillary membranes as easily as ions.58

Forceful inspiration against a closed glottis, such as occurs in laryngospasm, can result in a marked increase in negative intrathoracic pressures, as much as \(-140\) cm H\(_2\)O from a baseline average of \(-4\) cm H\(_2\)O.59 This pressure is transmitted to the pulmonary interstitium and increases venous return to the right side of the heart. When the hydrostatic pressure exceeds capillary oncotic pressure, fluid moves out of the capillaries into the pul- monary interstitial space. Normally, fluid is removed by the lymph vessels, but when the flow of fluid out of the capil- laries exceeds the capability of the lymphatic system, pul- monary edema results.

Persistent negative intrapleural pressure increases the formation of lymph in the lungs,60 and inspiratory resistance doubles the baseline lung-lymph flow in animal models.61 Lymphatics originate in the connective tissue spaces that surround the terminal bronchioles and then course to the hilum of the lung, emptying mainly into the right lymphatic or thoracic duct, which is then returned into the junction of the internal jugular and subclavian veins. Increased cen- tral venous pressures decrease the passive return of lymphatic fluid.62

Negative intrathoracic pressure increases venous return to the right side of the heart by decreasing right atrial pressure, caused by the transfer of negative intrathoracic pres- sure to the right atrial wall.63 The normal increase in venous return during inspiration is greatly increased in NPPE, so that the right ventricle may distend and impair filling of the left ventricle because of ventricular interdependence.64 In addition, the pericardium restricts overdistention of the heart chambers. End-diastolic left ventricular volume, stroke volume, and cardiac output all decrease.

The term pulsus paradoxus has been used to describe the situation in which an exaggerated decrease in systolic blood pressure occurs during inspiration. Normal pressure of the right ventricle is generally one fifth that of the left ven- tricle. The blood that flows into the lungs through several bronchial arteries amounts to about 1% to 2% of the total...
cardiac output. This blood, which is oxygenated—in contrast to the partially deoxygenated blood in the pulmonary arteries—is then shunted back to the left side of the heart without reoxygenation.

Decreased intrathoracic pressure is transmitted to the lungs, great vessels, and heart. An intrathoracic pressure decreased to –50 to –100 cm H₂O (–37 to –74 mm Hg) imposes an extra 37 to 74 mm Hg of work on the left ventricle to overcome during systole. The added work decreases cardiac output and subsequently increases pulmonary venous pressures.

After an initial increase in venous return with inspiration, a continuous inspiratory effort may result in the retardation or suspension of further venous return by compression of the great vessels at the thoracic inlet. The concept has been likened to attempting to suck on a collapsible straw. The decrease in venous return can be reflected to the left side of the heart as an increase in afterload, which can likewise be transmitted to the pulmonary veins and microvasculature.

Hypoxia and hypercarbia develop at the onset of NPPE. The sympathetic system releases catecholamines that cause the peripheral circulation to constrict and translocate systemic blood to the pulmonary circulation. Combined with increased venous return, this response increases capillary hydrostatic pressure and transudation into the interstitial space.

A hyperadrenergic response has also been reported in neurogenic and high-altitude pulmonary edema. In an experimental animal model, traumatic neurogenic pulmonary edema did not develop in animals treated with β-adrenergic blocking agents but did develop in untreated animals. The hypoxic, hyperadrenergic state also produces a loss of capillary integrity. Hypoxia further contributes to myocardial depression.

The volume of interstitial fluid in the lungs usually cannot increase by more than about 50%, or less than 100 mL, before the alveolar epithelial membranes rupture and fluid begins to move from the interstitial spaces into the alveoli. The normal volume of blood in the lungs is about 450 mL, or about 9% of the total blood volume. The Müller maneuver is an inspiratory effort against a closed glottis. The pulmonary interstitial hydrostatic pressure approximating the change in alveolar and pleural pressures becomes negative to about –100 cm H₂O, contributing to the high capillary transmural pressure. Clearly, there is little reserve before breakthrough occurs and pulmonary edema results.

Schwartz et al have suggested that the mechanism underlying NPPE, which they refer to as negative pressure pulmonary hemorrhage, is stress failure of the alveolar–capillary membrane caused by a marked elevation in pulmonary capillary hydrostatic pressure. When the alveolar–capillary membrane is viewed under the scanning electron microscope, stress failure is characterized by breaks in the capillary endothelial and alveolar epithelial barriers and the basement membrane. Although small increases in pulmonary capillary transmural pressure result in low-protein edema through alterations in the Starling forces, higher pressures cause ultrastructural changes in the capillary endothelial barrier and the development of exudative edema. Edema from increased capillary permeability may be related to physical damage from capillary distention, and also from the possible release of vasoactive substances such as kinins, histamine, and serotonin.

The use of crack cocaine is associated with pulmonary edema and hemorrhage and increased alveolar permeability, and it may contribute to the development of NPPE. Cardiac anomalies may also be a contributing factor. In 1 series, 3 of 6 patients with NPPE were found by echocardiography to have cardiac problems, including hypertrophic cardiomyopathy and tricuspid valvular insufficiency.

Structural cardiac anomalies are present in less than 1% of the general adult population. Right ventricular pressure may cause NPPE when a collapsed lung is expanded. Right ventricular pressure may occur more often when a lung has been collapsed for longer than 72 hours. Hydrostatic pressure can increase as a consequence of reperfusion and reactive hyperemia in a re-expanded lung, which develop in response to the negative intrapleural pressure used for lung re-expansion.

Pulmonary edema may also result from alterations in pulmonary vascular permeability caused by stretching of the pulmonary capillaries and hypoxia. Both increased hypoxic pulmonary vasoconstriction and altered capillary permeability contribute to the entry of fluids and proteins into the interstitial and alveolar spaces, which characterizes RPE. Other suggested causes of RPE include reduced production of surfactant and the effects of inflammatory mediators, including interleukin-8 and leukotrienes.

Signs and symptoms of RPE include dyspnea, chest pain, cough, rales, the production of pink frothy sputum, tachycardia, and hypotension. Measures to prevent RPE include limiting therapeutic suction pressure to –20 cm H₂O, limiting fluid removal to 1,500 mL, and reducing the speed at which fluid is removed.

Acute lung injury and ARDS may develop in severe cases of NPPE and RPE and may be accompanied by prolonged or refractory hypoxia. Hypoxia and metabolic acidosis are known myocardial depressants that may aggravate other causes of pulmonary edema. In children with asthma, a markedly negative transpulmonary pressure gradient has been shown to predispose them to the development of interstitial pulmonary edema. Because of the prolonged expiratory phase during an asthmatic attack, air trapping occurs, resulting in hyperinflation of the lung and a residual positive airway pressure at end-expiration. An “auto-PEEP” phenomenon may protect the alveoli from flooding during NPPE and mask the radiographic appearance of pulmonary edema during the obstructive event.

There is debate about the timing of the onset of pulmonary edema. Its development during or after relief of upper airway obstruction may depend on whether the obstruction is fixed or variable. Fixed upper airway obstruction would result in Valsalva and Müller maneuvers of equal magnitude, favoring the development of pulmonary edema after relief of the obstruction. Variable extrathoracic obstruction of the upper airway would worsen during the Müller inspiration, and pulmonary edema would develop during the period of obstruction.

**Treatment**

The first priorities in the treatment of NPPE are to relieve the airway obstruction and correct hypoxemia with supplemental oxygen. A patient with persistent hypoxia and airway obstruction requires intubation. Upper airway obstruction and laryngospasm are managed by nebulized adrenaline and positive end-expiratory pressure. Variable extrathoracic obstruction of the upper airway would worsen during the Müller inspiration, and pulmonary edema would develop during the period of obstruction.

Laryngospasm can recur. Preventive measures include oropharyngeal suctioning, the I.V. or topical administration of lidocaine, and allowing adequate recovery from anesthesia before extubation. Extubation while the patient is in a dependent anesthetic plane has been suggested to avoid laryngospasm. In a study of 299 patients (average age, 62 years), the incidence of laryngospasm did not differ between patients who were extubated under deep anoxia and those who were extubated after their airway reflexes were believed to have recovered. The study identified a higher incidence of airway obstruction due to dislodgment of the tongue against the posterior wall of the pharynx in patients extubated under deep anesthesia. In most reports of postobstructive pulmonary edema in children, the tracheal tube was removed while they were under deep anesthesia.

Therapeutic measures depend on the severity of hypoxemia. Sustained hypoxemia must be treated with an increased FIO₂ and mechanical ventilation with PEEP. Although diuretics have been given in the management of NPPE, caution must be exercised. Additional diuretics may cause hypovolemia and circulatory collapse. Up to 40% of the plasma volume may be translocated into the pulmonary circulation, with subsequent transudation into the interstitial and alveolar space. The role of diuretics in the management of NPPE should therefore be individualized.

Morphine may be used for sedation, increasing the vascular capacity and reducing venous return. Reintubation may be necessary in up to 85% of occurrences of NPPE. Holmes et al reported that only 1 of 8 patients with NPPE required prolonged intubation of 3 days; the single case was because of a delay in diagnosis. Among reintubated patients, 50% require continuous positive airway pressure or PEEP. Reintubation is facilitated with the use of neuromuscular blockers and sedatives to reduce laryngoscopy time and sympathetic stimulation.

If NPPE is recognized and treated promptly, most patients respond well, with a rapid resolution of the condition. Significant improvement is seen clinically and radiographically within 12 to 24 hours. In a series of patients, several subclinical cases of NPPE resolved without specific treatment. Some authors, however, have described less favorable outcomes. Goldenberg and colleagues reported 1 mortality in 6 cases of NPPE after otolaryngologic procedures, in the remaining cases, NPPE resolved within 24 hours.

Life-threatening complications occur and are attributed primarily to a delayed diagnosis. Patients whose condition does not resolve rapidly may have sustained pulmonary capillary damage secondary to mechanical disruption, prolonged hypoxia with acid–base and electrolyte imbalances, or hypotension. Bonadio and Losek noted that 2 of 5 children died after the development of pulmonary edema and respiratory failure caused by upper airway obstruction.

Kollef and Pluss described 1 death in 7 cases of NPPE. Such cases highlight the need for prompt recognition and treatment of this potentially dangerous condition.

An analysis of arterial blood gases is indicated if the patient requires mechanical ventilation. An arterial cannula and pulmonary catheter may be placed if the patient is hemodynamically unstable and the diagnosis is uncertain. In uncomplicated cases of suspected NPPE, pulmonary artery catheterization has revealed normal central venous pressures, pulmonary artery pressures, and pulmonary capillary wedge pressures. Pulmonary edema in patients with upper airway obstruction is associated with transient physiologic events; the immediate data obtained from a pulmonary catheter may be misleading. Urinary output should be measured because it is a good indicator of cardiac output and diuresis.

During mechanical ventilation, the use of excessive tidal volume and levels of PEEP greater than 10 cm H₂O can result in overdistention of the alveoli, rupture, and pneumothorax. The incidence of pneumothorax was found to be as high as 20% in a review by Tami et al. The use of high levels of PEEP must also be weighed against the possibility of reducing effective cardiac output.

Steroids may be useful in cases in which the airway is believed to be edematous following a difficult intubation or
a surgical procedure. However, the mechanism of action of steroids in facilitating the correction of pulmonary edema is not understood.

Many cases of NPPE have likely been misdiagnosed and treated as aspiration pneumonia. Each condition may present with different degrees of severity. Aspiration pneumonia and NPPE can both deteriorate to ARDS and multiple-organ failure. The initial treatment for both conditions is mechanical ventilation and PEEP. However, following flash aspiration, a release of cytokines and other vasoactive substances may accelerate the involvement of other organs.

Management of the Case Presented

The patient underwent tracheal intubation after receiving fentanyl, lidocaine, propofol, and rocuronium. Anesthesia was maintained with 50:50 oxygen-nitrous oxide and isoflurane. On his emergence from anesthesia, muscle relaxation was believed to be reversed. The patient was extubated after he reached for the endotracheal tube. Ventilation became difficult. Suxamethonium was administered, and he was then emergently reintubated. Pink frothy secretions immediately emerged from the endotracheal tube. The patient remained hypoxic with bronchospasm, believed to be caused by the increased airway pressures required to ventilate him. A 5-mg dose of morphine and a nondepolarizing muscle relaxant were administered. Epinephrine was used to treat the bronchospasm and bradycardia. (Epinephrine acts as a bronchodilator because of β2-adrenergic agonist effects and as a cardiac stimulant because of β1-adrenergic agonist effects.) As soon as the patient’s oxygen saturation had improved, he received lorazepam and propofol.

The patient’s lungs were mechanically ventilated with PEEP and respiratory nebulizer treatments for several days. The initial arterial blood gas measurements after reintubation indicated a pH of 7.24, a PaCO2 of 48 mm Hg, and a PaO2 of 1080. From the Hospital of the Rockefeller Institute for Medical Research.


LurchDG, SaitoSA. Post-excitation pulmonary oedema following anesthesia induced by upper airway obstruction: are certain patients at increased risk? Chest. 1984;90:802-805.


37. Bourke AM. Unilateral pulmonary oedema following postextubation laryngospasm. Anesthesiology News. This lesson is available online at www.mssm.procampus.net.
41. Bourke AM. Unilateral pulmonary oedema following postextubation laryngospasm. Anesthesiology News. This lesson is available online at www.mssm.procampus.net.

Post-test

1. Attempted inspiration against an obstructed airway results in all of the following physiologic responses except:
   a. increased venous return
   b. interventricular shift with decreased diastolic filling of the left ventricle
   c. transfer of systemic blood volume to the pulmonary circulation
   d. increase in diastolic volume of the left ventricle

2. The least likely risk factor for the development of negative pressure pulmonary edema (NPPE) is:
   a. a history of obstructive sleep apnea
   b. chronic airway obstruction secondary to adenotonsillar hypertrophy, masses, goiter, or acromegaly
   c. a full stomach
   d. being a muscular young adult

3. Chest X-ray findings in NPPE are most likely to include:
   a. an enlarged heart
   b. mediastinal shift of the heart
   c. decreased lung markings
   d. centralized distribution of pulmonary edema

4. The differential diagnosis of NPPE includes:
   a. cardiomyopathy
   b. sarcoidosis
   c. aspiration pneumonia
   d. pulmonary fibrosis

5. Attempted voluntary inspiration against a closed glottis is referred to as:
   a. Valsalva maneuver
   b. Müller maneuver
   c. Heimlich maneuver
   d. laryngospasm

6. Laryngospasm is caused by involuntary contraction of the:
   a. abductor muscles of the larynx
   b. thyroid muscles
   c. adductor muscles of the vocal cords
   d. vagus nerve

7. Collodium pressure of fluid movement across a semipermeable membrane is generat- ed primarily by:
   a. red blood cells
   b. sodium ions
   c. lower protein production and colloid pressure
   d. albumin

8. The lymphatic circulation is responsible for:
   a. negative pressure in the intrapleural space
   b. negative interstitial hydrostatic pressure
   c. resolution of third-spacing of fluid
   d. all of the above

9. Protection from NPPE in the elderly is a result of:
   a. an ability to generate high negative intrathoracic pressure
   b. susceptibility to increased capillary permeability edema
   c. lower protein production and colloidal pressure
   d. increased thickening of capillary-alveol membranes

10. The treatment of NPPE always includes:
    a. diuretics
    b. steroids
    c. angiotensin-converting enzyme inhibitors
    d. oxygen supplementation