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Case Scenario: Acute Postoperative Negative Pressure Pulmonary Edema

David J. Krodel, M.D.,* Edward A. Bittner, M.D., Ph.D.,† Raja Abdulnour, M.D.,‡ Robert Brown, M.D.,§ Matthias Eikermann, M.D., Ph.D.‖

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FORMATION of noncardiogenic pulmonary edema has been observed after a variety of inciting events, including upper airway obstruction (negative pressure pulmonary edema [NPPE]),[1] acute lung injury,[2] anaphylaxis,[3] fluid maldistribution,[4] and severe central nervous system trauma (neurogenic pulmonary edema).[5] Both the diagnosis of pulmonary edema and an understanding of its underlying pathophysiology have important implications for treatment. Patients with severe postoperative noncardiogenic pulmonary edema who require mechanical ventilation should be ventilated with a low-tidal volume,[6] administration of positive end-expiratory pressure, and low plateau airway pressures.[7,8] Recent studies suggest that noninvasive respiratory support might be a viable approach for the treatment of patients with postoperative respiratory dysfunction, including postoperative NPPE.[9]

Case Report

A 25-yr-old man (weight, 68 kg; height, 183 cm) presented to the surgery center for excision of back and thigh schwannomas on the same day. The patient's medical history was significant only for his history of multiple schwannoma resections and a history of smoking one pack of cigarettes per week for the past 5 yr. He denied previous problems with general anesthesia, and his baseline peripheral oxygen saturation was 99% on ambient air.

The patient was premedicated with 2 mg midazolam, and anesthesia was induced with 250 mg fentanyl, 500 mg thiopental, and 8 mg vecuronium given for facilitation of tracheal intubation. He was atraumatically intubated with a 7-mm ID endotracheal tube using a no. 3 Macintosh laryngoscope (Teleflex Medical, Research Triangle Park, NC) on the first attempt with direct visualization of the vocal cords. The patient was turned prone, bilateral breath sounds were reconfirmed, and schwannoma excisions were performed on the left thigh and the left flank. A total of 0.5 mg hydromorphone was administered for analgesia. The intraoperative course was unremarkable. The patient was hemodynamically stable with minimal blood loss and was easily ventilated and oxygenated. A total of 500 ml lactated Ringer's solution was administered during the 65-min surgical procedure. The pa-

* Resident, Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. † Instructor, Harvard Medical School; and Director, Critical Care Fellowship Program, Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School. ‡ Instructor, Pulmonary and Critical Care Unit, Department of Medicine, Massachusetts General Hospital, Harvard Medical School. § Professor, Departments of Anesthesiology and Critical Care Medicine; Environmental Health Sciences, Division of Physiology; Division of Pulmonary Medicine, Department of Medicine; and Department of Radiology; The Johns Hopkins University, Baltimore, Maryland. ‖ Assistant Professor, Harvard Medical School, and Universitaet Duisburg-Essen, Essen, Germany; and Director of Research, Surgical Intensive Care Unit, Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital.

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Address correspondence to Dr. Eikermann: Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School, Massachusetts General Hospital, 55 Fruit Street, Boston, Massachusetts 02114. meikermann@partners.org.

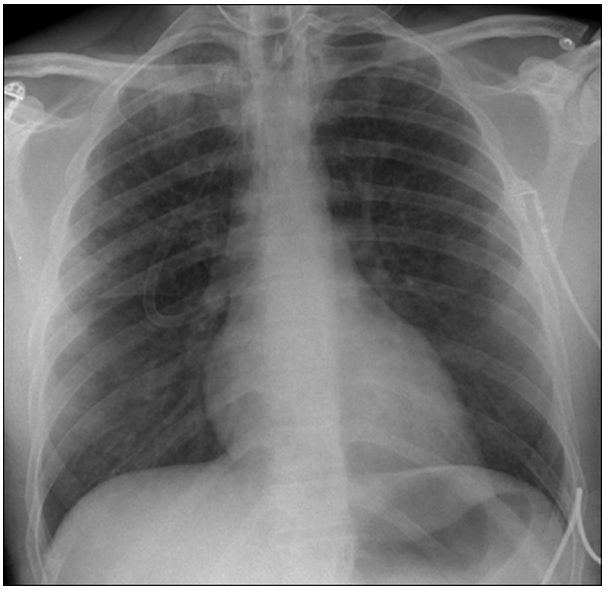

Fig. 1. Chest radiograph taken in the postoperative recovery room, revealing diffuse, bilateral, hazy, and interstitial opacity throughout both lungs, with increased visibility of small lung vessels, normal lung volumes, normal heart size, and no pleural effusions.

tient was returned to the supine position for emergence and extubation. Nondepolarizing motor blockade was not reversed because train-of-four monitoring of the ulnar nerve showed a train-of-four ratio of greater than 90%, demonstrating adequate spontaneous recovery.

Immediately after extubation, the patient developed inspiratory stridor consistent with laryngospasm; the anesthesiologist had difficulty in mask ventilating the patient, and peripheral oxygen saturation decreased to less than 80%. Laryngospasm was treated by 50 mg propofol and manual positive pressure mask ventilation with 100% inspired oxygen. Peripheral oxygen saturation improved gradually, and the patient was transported to the postanesthesia care unit for further supportive treatment.

In the postanesthesia care unit, the patient's oxygen saturation was maintained with 100% oxygen administered *via* a nonrebreather facemask. The patient coughed pink, frothy sputum during the course of the first postoperative hour. Physical examination revealed crackles bilaterally at the lung bases, and a chest radiograph was performed, showing diffuse, bilateral, hazy, and interstitial opacity throughout both lungs, with normal lung volumes, normal heart size, and no pleural effusions (fig. 1). A diagnosis of NPPE was made, and the patient was admitted to the inpatient postoperative recovery room for overnight observation. With supplemental oxygen, diuretic treatment, and bronchodilator inhalation, his respiratory status continued to improve with peripheral oxygen saturations greater than 94% on ambient air 10 h after surgery. Examination on the morning of the first postoperative day revealed clear lungs bilaterally and peripheral oxygen saturation of 95–97% on ambient air. He was discharged later that morning without signs or symptoms of respiratory compromise on oral analgesics and usual surgical follow-up in 1–2 weeks.

Discussion

Postoperative Recovery Room Diagnostic Evaluation and Treatment

A chest radiograph taken immediately after postanesthesia care unit admission showed diffuse bilateral opacities, a finding that was observed despite conservative intraoperative fluid management (fig. 1). The patient's history, operating room course, and clinical and radiologic findings were most consistent with pulmonary edema with NPPE as the likely cause; however, aspiration pneumonitis (Mendelsohn syndrome)[10] and diffuse alveolar hemorrhage resulting from upper airway obstruction[11] were also included in the differential diagnosis.

When considering the differential diagnosis of acute-onset perioperative pulmonary edema, both cardiac and noncardiac causes should be taken into account (table 1; fig. 2). Cardiogenic edema is usually preceded by new-onset left heart dysfunction and may be caused by acute ischemia, infarct, and/or severe arrhythmia, and the diagnosis is confirmed by echocardiography or measurement of the pulmonary artery occlusion pressure. It is likely that a combination of cardiogenic and noncardiogenic mechanisms contributes to the pathogenesis of postoperative pulmonary edema in many cases. For instance, although fluid overload itself can cause pulmonary edema in the presence of normal or even increased cardiac output,[12] intraoperative intravascular fluid overload can exacerbate chronic compensated heart failure.

Pulmonary edema caused by anaphylaxis is seen in the setting of exposure to a known or unknown allergen. In the perioperative setting, these often include neuromuscular blocking agents, antibiotics, anesthetics, or latex.[13] The onset is sudden and is typically accompanied by rash, urticaria, and swelling, but bronchospasm and hemodynamic collapse are frequently presenting symptoms. The clinical picture, time course, and severity, and its occurrence after administration of an allergen, help the clinician to relate signs and symptoms of pulmonary edema to an anaphylactic mechanism. The increased histamine and tryptase levels obtained immediately after the reaction are consistent with anaphylaxis. Radioallergosorbent tests and skin tests performed 4–6 weeks after a presumed reaction can help to confirm the clinical diagnosis and identify the inciting allergen.[13]

Neurogenic pulmonary edema typically occurs in the setting of a recent severe brain insult, such as subarachnoid hemorrhage, stroke, status epilepticus, trauma, or intracranial mass. Neurogenic pulmonary edema is typically accompanied by unregulated sympathetic discharge leading to pulmonary hypertension,[14] which induces stress failure of pulmonary capillaries and subsequent high permeability pulmonary edema.[15]

Table 1. Characteristics of Different Etiologies of Pulmonary Edema in the Perioperative Period

	Noncardiogenic					
	Negative Pressure	Anaphylaxis	Acute Lung Injury	Fluid Maldistribution	Neurogenic	Cardiogenic Left Heart Failure
Inciting factors	Laryngospasm Airway trauma OSA Oropharyngeal surgery Upper airway collapse Bronchial obstruction	Muscle relaxant Anesthetics Latex Antibiotics Intravenous contrast	Inflammation Aspiration Blood transfusions Pneumonectomy Pulmonary reperfusion Pulmonary reexpansion Toxic	Hypotonic fluid: TURP syndrome Isotonic fluid: Amniotic fluid embolism Tumescent liposuction	SAH Intraparenchymal bleeding Brain or spinal cord trauma Encephalitis Meningitis Hypoglycemia	Chronic CHF MI Arrhythmia
Clinical picture	Stridor/wheezing Hemorrhagic sputum	Hives Hypotension Wheezing	$Pa_{O_2}/F_{I_{O_2}}$ <300 mmHg Fever Regional decrease in breath sounds Rhonchi	Peripheral edema Confusion	Cranial hematoma Meningitis Confusion Focal neurologic signs	Distended jugular veins Oliguria Peripheral edema
Onset	Minutes	Minutes	Hours to days	Minutes	Hours	Minutes to hours
Duration	<24 h	<24 h	Days to weeks	<24 h	1 or more days	Variable
ECG	Normal or right heart strain pattern	Variable	Likely normal	Likely normal	Likely normal Maybe neuropathic ST changes	Dysrrhythmia, ST changes, and conduction defect
Laboratory findings	None specific	Increased S-tryptase levels	Edema fluid to plasma protein ratio >0.65	Hyponatremia Hypoosmolality	Hypoglycemia	Cardiac enzymes NT-pro BNP
Chest radiograph	Peripheral or central asymmetric peribronchial infiltrates	Diffuse bilateral pulmonary infiltrates	Diffuse bilateral pulmonary infiltrates	Diffuse bilateral pulmonary infiltrates	Diffuse bilateral pulmonary infiltrates	Central "bat wing" infiltrates Bilateral Kerley's B-lines

CHF = congestive heart failure; ECG = echocardiogram; Fi_{O_2} = inspired fraction of oxygen; MI = myocardial infarction; NT-pro BNP = N-terminal-pro brain natriuretic peptide; OSA = obstructive sleep apnea; Pa_{O_2} = arterial partial pressure of oxygen; SAH = subarachnoid hemorrhage; TURP = transurethral resection of prostate.

Acute respiratory distress syndrome and acute lung injury represent a heterogeneous group of severe hypoxic lung diseases. Activation of and damage to the pulmonary endothelium are the hallmark of acute lung injury or acute respiratory distress syndrome,[16] which is caused by a variety of inciting events such as sepsis, systemic inflammatory response syndrome, aspiration, caustic inhalation, blood transfusions, or trauma. Diagnosis is made by exclusion of other causes, as outlined in figure 2. The severity of hypoxic respiratory failure, chest radiographic findings, and the time course to recovery are key elements that need to be considered for making diagnosis of acute lung injury or acute respiratory distress syndrome. The edema fluid to plasma protein ratio is an additional method to discriminate between cardiogenic pulmonary edema and acute lung injury. Ware *et al.*[2] compared protein concentration (Biuret method) in the pulmonary edema fluid (taken *via* a suction catheter inserted into the endotracheal tube) and blood. Using a predefined cutoff of 0.65, the edema fluid to plasma protein ratio had a sensitivity of 81% and a specificity of 81% for the diagnosis of acute lung injury.

Before making the diagnosis of NPPE, other causes of pulmonary edema (table 2; fig. 2), particularly those requiring a rapid intervention (fluid maldistribution, anaphylaxis, and cardiogenic pulmonary edema), must be considered. In this patient, intraoperative fluid overload as a mechanism of pulmonary edema was not considered reasonable because the patient had only 500 ml isotonic solution administered intraoperatively, no history of left heart failure, and had been fasting overnight. There was no evidence of cardiogenic or neurogenic pathology and no signs or symptoms of anaphylaxis. Aspiration pneumonitis can be of increased concern in the prone position given the potential for increased abdominal pressure. Our patient was positioned on chest bolsters that allowed the abdomen to hang freely, which might help to decrease intraabdominal pressure. In addition, the radiologic picture of symmetric bilateral pulmonary interstitial infiltrates would be unusual for aspiration pneumonitis, which typically shows a localized infiltrate. In the immediate setting, we could not rule out acute lung injury or acute respiratory distress syndrome, but the severity of respiratory failure and the time course of clinical and radiologic recovery were not ultimately consistent with this etiology. Residual postoperative curarization is associated with reduced pharyngeal muscle tone and possible resulting upper airway obstruction.[17] In our patient, direct measurement of the train-of-four ratio by accelerometry showed a train-of-four ratio

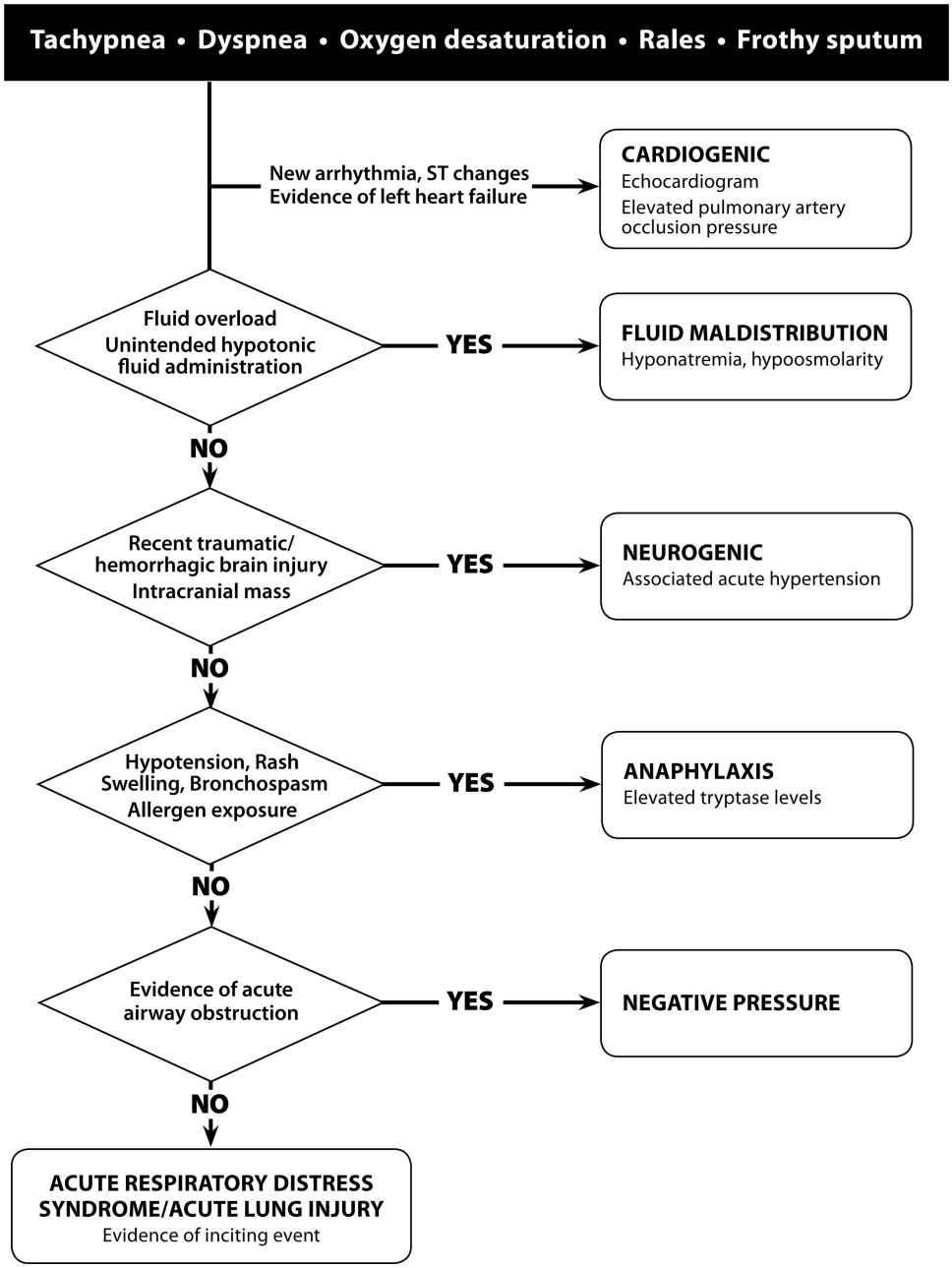

Fig. 2. An algorithm for the clinical differentiation of postoperative pulmonary edema. When considering the differential diagnosis of acute-onset perioperative pulmonary edema, both cardiogenic and noncardiogenic causes should be taken into account. Before making the diagnosis of negative pressure pulmonary edema (NPPE), other causes of pulmonary edema must be considered, particularly those requiring a rapid intervention (fluid maldistribution, anaphylaxis, and cardiogenic pulmonary edema). In the absence of evidence of upper airway obstruction typically leading to NPPE, an adult respiratory distress syndrome or an acute lung injury should be considered. Please note that the algorithm is based on clinical experience and has not yet been validated.

greater than 0.9, reflecting adequate recovery from muscle relaxant effects.[18] Coupling these considerations with the clinical picture of laryngospasm, we concluded that the patient's pulmonary edema was likely induced by negative intrathoracic pressure, potentially resulting from strong inspiratory efforts in the setting of laryngospasm.

In accordance with the reported data, symptoms and clinical signs of pulmonary edema resolved rapidly.[19] Although not performed in this patient, and typically unnecessary to make the diagnosis, hemodynamic measurements, including pulmonary artery occlusion pressure, pulmonary arterial pressure, and central venous pressure, taken after the development of edema, are typically normal.[20]

In this patient, conservative treatment with supplemental oxygen administered as 100% oxygen by a nonrebreather

Table 2. Negative Pressure Pulmonary Edema

Epidemiology
~1 in 1,000 patients receiving anesthesia
Postextubation, 74%
Laryngospasm
Patient bites on tracheal tube
During initial airway management, 26%
Head and neck tumors, 72%
Ludwig's angina, 14%
Laryngospasm, 14%
Pathophysiology
Highly negative intrathoracic (intrapleural) pressure generation
Increased venous return to right heart
Increased intrathoracic (pulmonary) blood volume
Increased pulmonary capillary permeability
Redistribution of fluid after relief of obstruction into pulmonary interstitium
Possibly increased capillary permeability
Clinical management
Airway/respiratory
Supportive respiratory care as needed to maintain adequate respiratory mechanics
Supplementary oxygen
Consider trial of NPS (CPAP, pressure support)
In severe cases of failing NPS, consider (re-)intubation
Pharmacologic
Consider administration of diuretics and/or inhaled β agonists
Outcome
Recovery in ~12–48 h assuming appropriate supportive measures are taken

CPAP = continuous positive airway pressure; NPS = noninvasive pressure support.

mask (flow, 15 l/min), 10 mg furosemide intravenously, and bronchodilators was started.[21] The patient's symptoms of pulmonary edema improved rapidly, such that noninvasive pressure support ventilation was not required. The rapid improvement of the patient's disease represents a typical case of acute postoperative pulmonary edema (table 2).

Epidemiology

Postoperative NPPE typically occurs in response to an upper airway obstruction, where patients can generate high negative intrathoracic pressures, leading to a postrelease pulmonary edema. The current literature regarding its epidemiology is sparse. Young, healthy, athletic patients seem to be at risk for this disorder,[22] and the prevalence of postoperative NPPE is approximately 0.1%.[22,23] In patients developing acute postoperative upper airway obstruction, NPPE has been reported at an incidence of up to 11% (table 2).[24]

Typical events leading to acute upper airway obstruction accompanied by perioperative NPPE include laryngospasm and endotracheal tube occlusion by biting. Less typically, NPPE can also occur after foreign body aspiration, oropharyngeal surgery, or postoperative residual curarization,[25] which typically impairs the upper airway dilator muscle strength while preserving inspiratory muscle function.[26] Case reports and retrospective data suggest that the patient characteristics that increase the risk of NPPE seem to include younger patients in American Society of Anesthesiologists physical status categories I and II, who are thought to be most capable of generating highly negative intrathoracic pressures during an obstructing event. Procedural characteristics increasing the risk of NPPE may include oropharyngeal surgery (especially for tumors or other potentially obstructing masses) although the true incidence and hazard ratios have not been reported.[23]

Pathogenesis of Noncardiac Pulmonary Edema

Diagnosis of noncardiogenic pulmonary edema requires an understanding of the pulmonary fluid homeostasis. The Starling equation describes the equilibrium of fluid flow through a semipermeable membrane:

$$Q = K[(P\text{mv} - P\text{pmv}) - (\pi\text{mv} - \pi\text{pmv})],$$

where Q = the net transvascular flow of fluid, K = the membrane permeability, Pmv = hydrostatic pressure in the microvessels, Ppmv = hydrostatic pressure in the perimicrovascular interstitium, πmv = plasma protein osmotic pressure in the peripheral vessels, and πpmv = protein osmotic pressure in the perimicrovascular interstitium.

The osmotic pressure is exerted by solutes in the blood *versus* those in the interstitium, which cannot cross the semipermeable membrane. Under normal conditions, most of this filtered fluid from the capillaries is returned to the systemic circulation by lymphatics.[27] The alveolar spaces, because of tight junctions in the alveolar epithelium, have very low permeability and do not fill with fluid. Disturbances of pulmonary fluid homeostasis can be induced by four pathways that can lead to increased interstitial fluid: increased hydrostatic pressure in the pulmonary capillary bed (or conversely, decreased pressure in the interstitium), decreased osmotic pressure of plasma, increased permeability of the membrane, and decreased return of fluid to the circulation *via* lymphatics.[27,28]

Pathogenesis of NPPE

During upper airway obstruction and forceful inspiration, pressure in the trachea and lower airways will decrease markedly. The pressure in the pleural space decreases by exactly the same amount, and the pressure in the pulmonary vessels decreases by much less, thus increasing the pressure difference between inside and outside the capillaries and accelerating the formation of interstitial fluid.

Two different mechanisms may explain the development of pulmonary edema during airway obstruction. The most likely mechanism relates to the observation that high negative intrathoracic pressures cause significant fluid shifts from the microvessels to the perimicrovascular interstitium, as seen in patients with congestive heart failure or fluid maldistribution states. The second proposed mechanism involves the disruption of the alveolar epithelium and pulmonary microvascular membranes from severe mechanical stress, leading to increased pulmonary capillary permeability and protein-rich pulmonary edema.

Evidence for a hydrostatic mechanism of NPPE comes from experimental and clinical data.[29,30] In an experimental model of NPPE, Loyd *et al.*[29] induced a negative inspiratory pressure in sheep (a 9 mmHg decrease in mean central airway pressure). Left atrial pressure decreased by 8 mmHg, and lung lymph flow was increased twice at baseline. Pulmonary arterial pressure was unchanged. The authors concluded that inspiratory loading is associated with an increase in the pulmonary transvascular hydrostatic gradient, possibly by causing a greater decrease in interstitial pressure than in microvascular pressure. Healthy human subjects can generate very high levels of negative inspiratory pressure (>100 mmHg), which in turn increases the return of blood to the right side of the heart, concomitantly increases pulmonary venous pressures, and decreases "downstream" pulmonary interstitial perivascular pressure. The negative intrathoracic pressures generated during the Mueller maneuver (inspiratory effort against a closed glottis) will result in an increased afterload,[31] which in turn will augment the pulmonary capillary hydrostatic pressures. Consequently, a marked increase in hydrostatic pulmonary pressure gradient can be generated, such that fluid filters out of the microcirculation and into the lung interstitium. When a critical quantity of edema fluid collects in the interstitial compartment, alveolar flooding occurs.[32]

Clinical Management

Although many patients with NPPE recover with conservative management as in this case, some patients with severe NPPE (or underlying cardiopulmonary disease) require temporary intubation and mechanical ventilation with positive end-expiratory pressure.[33] Diuretics are often administered, but their use is controversial and may even be unnecessary.[19]

The patient's wheezing was thought to represent bronchoconstriction, which we treated with inhaled bronchodilators; however, wheezing is caused by air flow through narrowed airways, and this may not necessarily be due to bronchospasm. Turbulence within bronchi, irrespective of the cause, including interstitial edema induced narrowing of bronchial lumina, may account for the development of the clinical symptom wheezing. *In vitro* and *in vivo* studies in human and animal models show that β agonists may increase the rate of alveolar fluid clearance *via* increased active cation transport.[34] Although it is unclear how much nebulized salbutamol arrived at the alveolar epithelium in our patient, it is possible that bronchodilator administration may have accelerated regression of symptoms of pulmonary edema.

An alternative to intubation is noninvasive respiratory support (*i.e.*, noninvasive positive pressure ventilation or treatment with continuous positive airway pressure). Recent data suggest that noninvasive respiratory support may be an important tool to prevent or treat acute respiratory failure while avoiding intubation. The aims of noninvasive respiratory support in the context of NPPE include: to partially compensate for the affected respiratory function by reducing the work of breathing; to improve alveolar recruitment with better gas exchange; and to reduce left ventricular afterload, increasing cardiac output and improving hemodynamics.[35] Evidence suggests that noninvasive respiratory support may be an effective strategy to reduce intubation rates, intensive care unit and hospital lengths of stay, and morbidity and mortality in postoperative patients.[9,35] Ultimately, NPPE is a generally benign condition typically resulting in full recovery in 12–48 h when recognized early and necessary supportive treatment is instituted for hypoxemic and/or hypercapnic respiratory failure.

Knowledge Gap

The immediate consequence of the Mueller maneuver is a markedly negative intrathoracic pressure, leading to increased pulmonary transvascular hydrostatic pressure and vulnerability to accumulation of filtered fluid in the interstitium and, ultimately, in the alveoli.

In addition to a hydrostatic mechanism of NPPE, there is evidence that the increased wall stress (circumferential wall tension caused by the transmural pressure) will alter the permeability coefficient (K) of the endothelial barrier. A classic paper by John B. West, M.D., Ph.D., D.Sc. (Distinguished Professor of Medicine and Physiology, School of Medicine, University of California, San Diego, San Diego, California), *et al.*[36] studied the effects of increased capillary transmural pressure in isolated rabbit lungs. The number of breaks in the endothelium increased with perfusion pressures, suggesting that high capillary hydrostatic pressures cause major changes in the ultrastructure of the walls of the capillaries, leading to a high-permeability form of edema. This suggestion was subsequently translated into a human model of increased capillary transmural pressure. This study was performed in six healthy athletes 1 h after an extensive cycling exercise. Analysis of bronchoalveolar lavage in healthy athletes after cycling exercise revealed a higher erythrocyte count and increased protein and albumin content compared with controls, indicating disruption of the endothelial membrane and stress failure. This suggests that acute increases in transmural pressures such as in NPPE may lead to increased permeability of the endothelial barrier.[37]

Some information is available on the molecular mechanisms involved in increased endothelial barrier permeability in response to wall stress. When an acute increase in transmural pressure occurs, the radial expansion of the capillary wall translates into linear cellular stretch. Compared with shear stress from laminar flow, the response of endothelial cells to linear stretch is maladaptive.[38,39] Oxidative stress is one mechanism for injury that seems to be up-regulated by increased linear stretch. In fact, increasing levels of cyclic linear stretch result in up-regulation of inducible nitric oxide synthase[40] and xanthine oxidoreductase, as has been shown by Abdulnour *et al.*,[41] both of which have been repeatedly implicated in cellular injury and increased vascular perme-

ability. Future studies will show whether these mechanisms of increased vascular permeability are clinically relevant in patients presenting with NPPE.

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ANESTHESIOLOGY REFLECTIONS

The Morton House II by Vandam

History tells us that the etherizer who first *publicly* demonstrated surgical anesthesia was William Thomas Green Morton (1819–1868). However, the muse Clio seems confused as to whether Morton was born at the site above on August 9 or 19. A retired Editor of ANESTHESIOLOGY, watercolorist and anesthesiologist Leroy D. Vandam (1914–2004), after visiting Morton's birthplace, had observed that the "original Morton house was a large, square old-fashioned wooden house on a farm that was deeded to William Thomas Green Morton's mother, Rebecca, by her father, John Stevens." Because the original Morton house had burned, its successor was the edifice (*above*) that Professor Vandam captured with watercolors. As a benefit for the Wood Library-Museum, just a few of the 100 prints signed by the late Dr. Vandam remain available for sale. (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

George S. Bause, M.D., M.P.H., Honorary Curator, ASA's Wood Library-Museum of Anesthesiology, Park Ridge, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.

Questioning Diuretic Use in Acute Negative-pressure Pulmonary Edema

To the Editor:

In their case study of negative-pressure pulmonary edema (NPPE), Krodel *et al.*[1] repeat the oft-cited idea that diuretics should be included in the therapies for this condition. They refer to using furosemide in the postanesthesia care unit for NPPE, which occurred as a result of laryngospasm on emergence. The authors do acknowledge that diuretics are not universally recommended for NPPE, noting that they "are often administered, but their use is controversial and may even be unnecessary." However, we are surprised that expert opinion continues to afford even a qualified role to diuretics. To our knowledge, there has never been any evidence for doing so. Beyond the knee-jerk association between pulmonary edema and loop diuretic administration, we cannot imagine why NPPE should routinely or even occasionally be managed with diuretics. Indeed, the careful elucidation of pathophysiologic features in this review should demonstrate that neither intravascular nor total body volume is increased in those with NPPE; these volumes, in contrast, may be significantly decreased. The sudden shift of fluid into the pulmonary interstitium has little in common with other scenarios in which diuresis is helpful in reducing excess total body water. In those with NPPE, diuretic administration may be unnecessary and harmful, particularly in patients who are older and less able to compensate for hypovolemia than the 25-yr-old otherwise healthy man who is described. Indeed, anecdotal experience at our institution has shown that furosemide administration to patients with NPPE can result in hypovolemic shock requiring fluid resuscitation.

Bryan G. Maxwell, M.D., M.P.H.,* Frederick G. Mihm, M.D. *Stanford University Medical Center, Stanford, California. bmaxelll@stanford.edu

Reference

1. Krodel DJ, Bittner EA, Abdulnour R, Brown R, Eikermann M: Case scenario: Acute postoperative negative pressure pulmonary edema. ANESTHESIOLOGY 2010; 113:200–7

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Acute Postoperative Negative-pressure Pulmonary Edema

To the Editor:

We read with interest the case scenario regarding acute postoperative negative-pressure pulmonary edema (NPPE).[1] The authors elegantly discussed the diagnosis, differential diagnosis, epidemiological features, pathogenesis, and clinical management of NPPE. We are concerned that anesthetic management may have inadvertently contributed to the cause of this complication. The patient described was given opioid doses equivalent to 27.5 mg iv morphine (0.25 mg fentanyl = 25 mg + 0.5 mg hydromorphone = 2.5 mg)[2] and a nondepolarizing muscle relaxant. The fact that the patient (with a normal airway) developed laryngospasm after extubation suggests that the patient was not ready for extubation. In addition, it is possible that reduced pharyngeal muscle tone due to residual neuromuscular blockade resulted in upper airway obstruction.[3,4] A patient with a "train-of-four" ratio of 0.9 or greater may still develop postoperative hypoxemia[5] and may require the administration of reversal drugs.

The initial difficulty in mask ventilation after extubation implies that the inspiratory stridor had progressed to a ball–valve obstruction.[6] Applying positive airway pressure under these circumstances may actually worsen ball–valve closure.[6] Inflation of the pharynx distends the piriform fossae, pressing the aryepiglottic folds more firmly against each other and reinforcing the closure.[6]

We suggest that the complication presented could have been prevented by delaying extubation.

M. Ramez Salem, M.D.,* Kenneth D. Candido, M.D., Arjang Khorasani, M.D. *Advocate Illinois Masonic Medical Center, Chicago, Illinois. mrsalem@sbcglobal.net

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In Reply:

The comments of Drs. Maxwell and Mihm invite a further discussion of diuretic use in the setting of postoperative negative-pressure pulmonary edema (NPPE).[2] Although diuretics were administered to the patient in our case, as originally stated, it is debatable whether this therapy benefited the patient in the case scenario.

In NPPE, the primary problem is not fluid overload but a combination of negative intrathoracic pressure–induced fluid shifts from the microvessels to the perimicrovascular interstitium (hydrostatic edema, as seen in patients with congestive heart failure) and disruption of the alveolar epithelium and pulmonary microvascular membranes from severe mechanical stress (high-permeability edema, as seen in patients with acute lung injury).[1] Diuretic therapy is a key component of hydrostatic pulmonary edema therapy, and it is being used for treatment in some patients with acute lung injury. In the euvolemic patient with NPPE, diuretic treatment is usually not required because most patients recover quickly after the airway obstruction is resolved. However, because NPPE is a diagnosis of exclusion, a single dose of diuretic under appropriate monitoring while a final diagnosis of NPPE is determined may be reasonable to treat causes of pulmonary edema that would be responsive to diuresis.

Salem *et al.* bring up the important question of how to determine whether a patient is "ready" for extubation. We argue that any patient developing NPPE after extubation, in retrospect, obviously was not ready for extubation: laryngospasm and retroglossal airway obstruction occur infrequently in the calm, completely awake, neuromuscularly intact patient with minimal oropharyngeal secretions. We administered 250 μg fentanyl to a young patient for a 65-min procedure. Despite the ability to follow commands, it remains possible that some degree of narcosis contributed to the clinical situation, although case series of NPPE have not yet identified this as a major risk factor.[3]

With respect to neuromuscular blockade, we agree that full neuromuscular blockade recovery is necessary before extubation to prevent upper airway obstruction due to pharyngeal muscle weakness in the presence of a neuromuscularly intact diaphragm. Several previous studies have demonstrated that a train-of-four ratio greater than 0.9–1 predicts recovery of the pharyngeal musculature, resulting in reduced postoperative upper airway obstruction, postoperative hypoxemia, and shorter postanesthesia care unit length of stay; a train-of-four of 0.9 represents the best available evidence to indicate adequate recovery of respiratory function from the effects of nondepolarizing neuromuscular blocking agents.[4] Furthermore, reversal agents and anticholinergics are known to have documented cardiovascular and respiratory adverse effects.[5,6] It was recently shown that 2.5 mg neostigmine coadministered with glycopyrrolate, when given after full recovery, increases upper airway collapsibility and impairs genioglossus muscle activation, further supporting the notion that quantitative measurement of neuromuscular blockade is crucial to the decision to administer reversal agents before extubation.[7] For these reasons, we strongly believe that reversal agents in the presence of full neuromuscular blockade recovery should not be given.

David J. Krodel, M.D., Matthias Eikermann, M.D., Ph.D.* *Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, and Universität Duisburg-Essen, Germany. meikermann@partners.org

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Face Mask Ventilation Using a Lower Lip Face Mask Placement in Edentulous Patients

To the Editor:

The recent article of Racine *et al.*,[1] which compared face mask ventilation using mandibular groove and lower lip placement in edentulous patients, was of great interest to us. Although the technique they describe appears interesting, one technical clarification is required regarding face mask ventilation using a lower lip placement with two hands. We

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