Exhaled-Breath Condensate pH Can Be Safely and Continuously Monitored in Mechanically Ventilated Patients

Brian K Walsh RRT-NPS RPFT, Dan J Mackey MD, Thomas Pajewski MD PhD, Yuanlin Yu MD, Benjamin M Gaston MD, and John F Hunt MD

BACKGROUND: Airway inflammation in acute and chronic respiratory diseases is characterized in part by abnormal pH in airway-lining fluid. The pH of exhaled-breath condensate (EBC) is low (acidic) in various pulmonary inflammatory diseases, including asthma, chronic obstructive pulmonary disease, cystic fibrosis, pneumonia, and acute respiratory distress syndrome. Because the time course of pH changes in the airway is not yet clear, we aimed to develop a method for frequent and intensive EBC pH data collection in mechanically ventilated patients. METHODS: We examined the collection, gas-standardizing (CO_2 removal), and continuous monitoring of pH of EBC from the expiratory port of a Servo-i ventilator with mechanically ventilated patients. We developed a condensing device that attaches to the exhaust port and is chilled by an electric cooling system. We built a 2-chamber gas-standardization and pH-measuring device that attaches to the condensing system and records pH every 6 s. After safety testing, we enrolled mechanically ventilated patients (with diverse reasons for requiring ventilatory support) for up to 96 h of continuous EBC pH condensimetry. RESULTS: The pressure, volume, and flow of the ventilator attached to a test lung were unchanged by application of the condensimeter, at various flows (2–120 L/min) and ventilator settings. We monitored 19 pediatric patients for 6–96 h. The pH of the accumulated EBC in the storage container correlated with the geometric mean of all the pH data points from the condensimeter during the recording period ($r^2 = -0.95$, $p < 0.001$), which internally validated that the condensimetry system provides accurate, well gas-standardized readings for up to 96 h. The EBC pH values were similar to published reports of single samples. The EBC pH became more acidic during clinical deterioration and normalized with recovery. CONCLUSION: Continuous monitoring of EBC pH from the ventilator exhaust port is safely achievable and reliably provides data that may become useful in monitoring critically ill patients. *Key words: exhaled-breath condensate, pH, airway inflammation, respiratory disease, condensimetry.* [Respir Care 2006;51(10):1125–1131.

Introduction

Exhaled breath contains aerosols and vapors that can be collected by condensation, and analyses of the characteristics and content of this exhaled-breath condensate (EBC) have revealed numerous differences between healthy and diseased patients.[1] To collect EBC, the exhaled gas is passed through a condensing apparatus, resulting in precipitation. This EBC "rainout" predominantly consists of water vapor. However, it has dissolved within it compounds derived from the airway-lining fluid, including water-soluble volatile compounds—some of which are acidic—and diverse nonvolatile compounds, including cytokines, surfactant, salts, oxidants, and small-molecular-weight biologically active mediators such as adenosine.[2] It is the ability to trap acids that allows EBC to shed light on what

SEE THE RELATED EDITORIAL ON PAGE 1118

Brian K Walsh RRT-NPS RPFT, Dan J Mackey MD, Yuanlin Yu MD, Benjamin M Gaston MD, and John F Hunt MD are affiliated with the Department of Pediatrics; Thomas Pajewski MD PhD is affiliated with the Department of Anesthesiology, University of Virginia, Charlottesville, Virginia.

This research was funded by the University of Virginia Children's Hospital and the United States Air Force.

has previously been a dark room: the pH of the airway-lining fluid in health and disease.

Many proteins and cells in the airways have functions that are critically pH-dependent. Although not explored until recently, the airway possesses mechanisms to maintain pH homeostasis,[3] for the toxicities of unregulated airway acidification are numerous.[4] For example, chlorine-gas inhalation acidifies the airway (through formation of hydrochloric and hypochlorous acids), and the symptoms of chlorine toxicity mimic the wheezing, coughing, and dyspnea of asthma.[5]

What constitutes a healthy airway-lining-fluid pH is beginning to become clear. The literature on invasive pH probe measurements and tracheobronchial-secretion measurements indicates that airway pH in health is maintained mildly alkaline, with a pH of 7.5–7.8.[4] Because of the potential adverse effect of probing the airway, there are few invasive airway pH data in disease states, but what data there are suggest prominent acidification of the airway-lining fluid during disease.[6] EBC can provide information about airway-lining fluid pH in disease, by leveraging the fact that acidic compounds, such as formic acid and acetic acid, are only volatile from acidic source fluids. EBC traps these volatiles, and the EBC pH is then reduced when airways are acidified. This was demonstrated in a bovine model of airway acidification, in which invasive pH probe and EBC pH measures correlated well.[7]

Gas-standardization to control for CO_2 is an important component of the EBC pH assay. The exhaled CO_2 level tells us nothing about the pH of the airway-lining fluid, but serves as a precursor to the formation of carbonic acid in solution, which acidifies EBC, creating "noise" in the system. The acid formed from CO_2 dissolution affects the pH of the EBC more than it affects the pH of the more buffered airway-lining fluid. A process of gas-standardization (which removes most dissolved CO_2 and therefore the acidity contributed by carbonic acid) allows for other acids to become clearly evident in the EBC pH assay, by increasing the ratio of the signal (volatile acids in EBC) to noise (carbonic acid formed from CO_2). These volatile acids (acetic, formic, and others) are the signal of interest, because they are specifically volatile from acidic source fluids (unlike CO_2), so their presence in the EBC reflects acidic airway-lining fluid. Removal of contaminating CO_2 improves the reproducibility and stability of the EBC pH assay and increases the assay's utility to assess airway pH. In practice, gas-standardization is accomplished by fully equilibrating EBC with a CO_2-free gas such as argon, nitrogen, or oxygen.[8] Using this gas-standardization, investigators have demonstrated that the pH of EBC is low (acidic) in multiple pulmonary inflammatory diseases, including asthma, chronic obstructive pulmonary disease, cystic fibrosis, and acute respiratory distress syndrome.[4,8–11]

Acidification of tracheal fluids and exhaled breath occurs prior to clinical recognition of ventilator-associated pneumonia.[12] We sought to determine if EBC pH can provide similar prognostic information, so we developed a system to provide continuous gas-standardized EBC pH monitoring in intubated patients. We refer to this system as continuous pH condensimetry. We performed continuous pH condensimetry in 19 intubated patients, and here we report for what we believe to be the first time a technique that can rapidly and continuously track the development and resolution of airway acidification.

Methods

Subjects

The control subjects were lung-healthy, nonsmoking patients undergoing elective surgical procedures with intravenous (noninhalational) anesthesia, and they were recruited in the preoperative suite at the University of Virginia. Ill subjects were recruited from the intensive care units. All patients (or their guardians) provided informed consent, and the studies were approved by the university's human investigation committee.

Collection of EBC From the Mechanical Ventilator

The ventilator exhaust port normally expels hot humid air into the patient's room, especially when an active humidification device with heated expiratory limb is incorporated in the ventilator circuit. Our system passes the exhaled gas through a condenser, passes the condensate through 2 gas-standardization chambers, then passes the gas-standardized condensate over a pH-measurement probe.

We compared the gas-standardized pH of EBC collected from patients' endotracheal tubes (ETTs) with matched samples collected approximately 2 m downstream in the exhalation circuit and/or the ventilator exhaust port, to determine if distance from the ETT and the presence of

John F Hunt MD, Benjamin M Gaston MD, and Brian K Walsh RRT-NPS RPFT are inventors of intellectual property relating to exhaled-breath-condensate pH measurement techniques.

John F Hunt MD and Benjamin M Gaston MD are co-founders of Respiratory Research Inc, Charlottesville, Virginia, which manufactures exhaled-breath condensate collection systems.

Brian K Walsh RRT-NPS RPFT presented a version of this paper at the 51st International Respiratory Congress of the American Association for Respiratory Care, held December 3–6, 2005, in San Antonio, Texas.

Correspondence: Brian K Walsh RRT-NPS RPFT, Box 801352, Division of Pediatric Respiratory Medicine, University of Virginia, Charlottesville VA 22908. E-mail: bkw2j@virginia.edu.

humidified bias flow affects EBC pH. The breathing gas was heated and humidified (model 850, Fisher Paykel Healthcare, Auckland, New Zealand), and we tested pediatric and adult ventilator circuits with heated expiratory limbs. Individual EBC samples were collected using a valveless modification of a commercial portable EBC collection device (RTube, Respiratory Research, Charlottesville, Virginia) incorporated directly into the circuit or attached to the ventilator exhaust port for 10 min, while cooled to an initial temperature of 0°C. EBC pH was measured after gas-standardization with argon gas for 8 min, as previously reported.[13]

Continuous pH Condensimetry System

We developed a device that attaches to the exhaust port of the Servo-i ventilator (Maquet, Bridgewater, New Jersey) and continuously condenses the expired air, gas-standardizes the collected EBC, and constantly monitors the EBC pH as it flows, milliliter by milliliter, out of the system and into a waste container. The condensimeter cools the exhaled air from the heated expiratory limb, using an aluminum condenser surface kept continuously chilled to 5° C by circulated cold water (Electra Cool II, Cincinnati SubZero, Cincinnati, Ohio).

EBC is collected by gravity into 2 serial collection chambers. In the first chamber, CO_2 is removed from the EBC by equilibrating the continuously collecting EBC with a constant flow of oxygen (60 mL/min) bubbled through the sample. As fresh EBC enters this chamber, collected sample overflows into a lower (second) chamber, and an additional 30 mL/min of oxygen is bubbled into the sample to further equilibrate it. In this second chamber the pH is measured by a glass micro combination pH electrode (Orion 9803, Thermo Electron, Waltham, Massachusetts) as it exits the system. No more than 1.1 mL of EBC is in the assay chamber at any time, and this chamber is constantly receiving freshly collected EBC from the condenser.

The pH probe is connected to a 9-volt pH recorder (Flexilog 2000, Oakfield Instruments, Morrisville, North Carolina) that measures pH every 6 s, for a maximum recording period of 96 h (Fig. 1). Calibration of the pH probe is performed with low-ionic-strength buffers before each monitoring session, and a post-calibration is performed to determine if there was deviation during the recording period.

Prior to use with patients, we studied the condensimeter's effects on ventilator-performance characteristics and resistance at multiple flow rates (2–120 L/min) and settings. We monitored pressure, volume, flow/time graphics, and digital readings before and after applying the condensimeter to a Servo-i ventilator. A second sensor device for monitoring flow, pressure, and volumes (NICO, Respironics, Carlsbad, California) was inserted at the test lung.

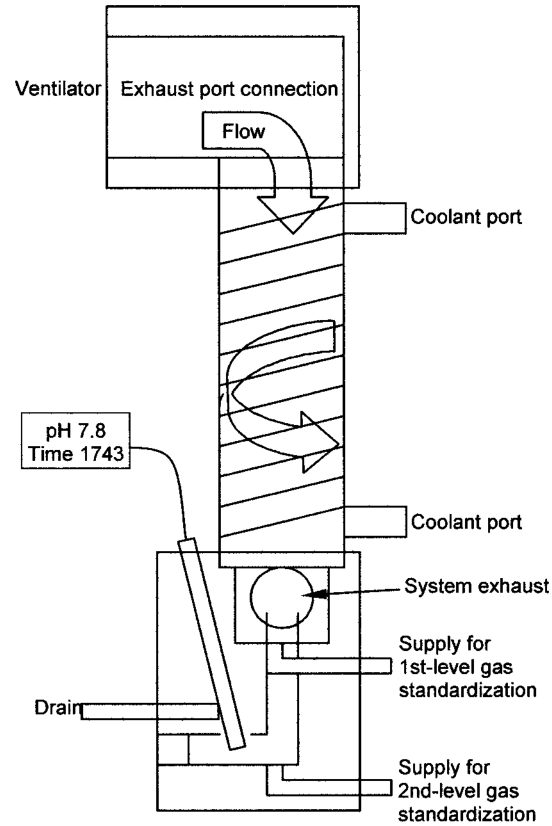

Fig. 1. Diagram of the condensimeter, used to collect and perform continuous gas-standardization and pH measurement on exhaled-breath condensate.

Internal Validation

We retained all EBC that had been collected into the waste container during continuous EBC pH monitoring. This accumulating volume was stored at room temperature until the condensimeter was removed from the ventilator. We compared the pH of the accumulated EBC in the storage container with the geometric mean of all the EBC pH data points from the condensimeter during the recording period, which amount to effectively continuous (but, in fact, every-6-s) measurement of EBC pH.

We additionally performed continuous pH measurements of humidifier water passing through an adult circuit (Fisher Paykel Healthcare, Auckland, New Zealand) propelled by bias flow air, without a patient in the circuit. We compared the gas-standardized pH value of the sterile water in the humidifier chamber to the EBC pH collected distal to the expiratory limb over a period of 11 h.

Statistical Calculations

The gas-standardized EBC pH values from the ETT and from the distal portion of the expiratory limb/exhaust port

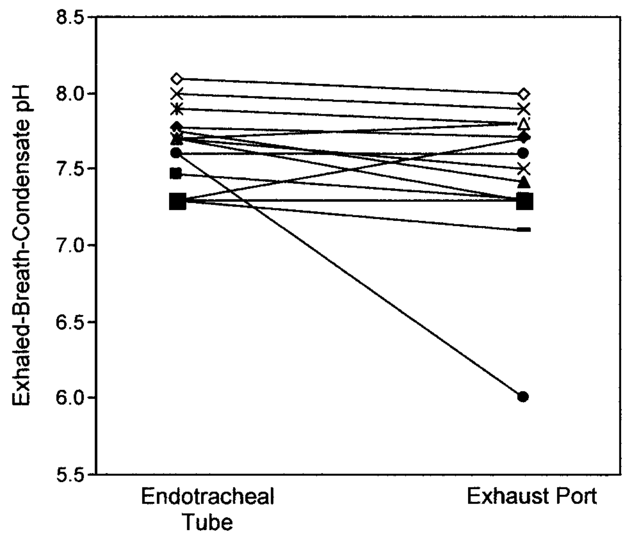

Fig. 2. Comparison of gas-standardized pH of exhaled-breath condensate (EBC) samples obtained from the endotracheal tube and samples collected approximately 2 m distally in the ventilator's exhalation circuit/exhaust port. The collections were performed 10 min apart, and they show no significant difference. Note the sharp decline in one of the data pairs, which might indicate an aspiration event.

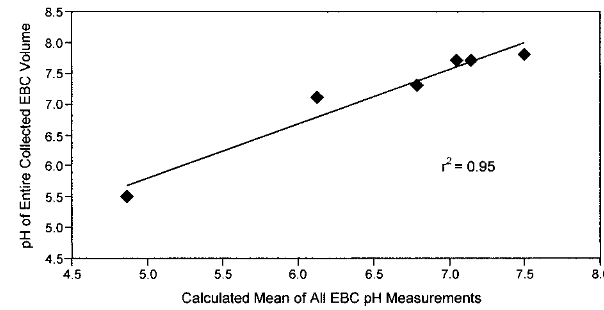

Fig. 3. Correlation between the mean recorded exhaled-breath condensate (EBC) pH during the entire continuous condensate-sampling period and the gas-standardized pH of the total collected volume of the condensate. This serves as internal validation of the system and helps to identify the relevance of any calibration drift.

were compared with the Wilcoxon signed rank test (SigmaStat 3.0, SyStat Software, Point Richmond, California). We graphically analyzed the EBC pH measurements with the graphing feature in a spreadsheet program (Excel, Microsoft, Redmond, Washington). The pH of the total collected EBC and the geometric mean of all the individual EBC pH measurements were examined with the correlation coefficient (r^2).

Results

ETT Versus Exhaust-Port EBC pH Values

There was no significant pH difference between the 15 EBC samples collected directly from the ETT (7.70, 25–75% range 7.50–7.76) and the matched samples collected subsequently approximately 2 m down the expiratory limb/exhaust port (7.60, 25–75% range 7.30–7.80) ($p = 0.22$) (Fig. 2). Note, however, that one exhaust-port collection had a substantially lower EBC pH than its preceding direct endotracheal collection, the explanation for which is not certain.

Effects of the Condensimeter on Ventilator Function

There were no changes in flow, pressure, or volume characteristics at any ventilator settings on addition of the condensimeter to the exhaust port.

Internal Validation

There was a significant correlation ($r^2 = 0.95$, $p < 0.001$, $n = 6$) between the pH of the total mixed EBC collected in the waste container and the geometric mean of all individual pH measurements (up to 57,600 individual measurements) during the recording periods (Fig. 3). This confirms that substantial artifact is not present in the pH measurement or recording system.

Without a patient in the circuit, there was a completely steady EBC pH value of 5.6 over a period of 11 h, which was equivalent to the measured pH of the sterile water in the humidifier.

EBC pH Values From Patients

We enrolled 19 mechanically ventilated patients with various degrees of lung health for continuous pH condensimetry. Causes of respiratory failure included acute infection with respiratory syncytial virus (2 patients), acute respiratory distress syndrome (3 patients), pneumonia (2 patients), asthma (1 patient), tracheal stenosis with reconstruction (3 patients), cystic fibrosis (1 patient), primary pulmonary hypertension of the newborn (1 patient), status post-spinal-fusion (2 patients), and congenital heart disease (1 patient with atrioventricular canal, 1 with patent ductus arteriosus, 1 status post-heart-transplant, 1 mitral-valve replacement). The patients' ages ranged from 5 days old to 17 years old (Table 1).

The duration of pH condensimetry ranged from 7 h to 96 h. There were no adverse events related to the presence of the condensimeter on the exhaust port. During some of the more prolonged condensimetry recordings (over 48 h) there was a mild degree of pH-probe calibration drift, although in shorter recording periods this was never an issue.

Table 1. Patient Age, Diagnoses, and Duration of Condensimetry Monitoring

Patient Number	Age	Diagnosis and Contributing History	Duration of Condensimetry (h)
1	17 y	Head trauma, acute brain injury	23
2	9 mo	Respiratory syncytial virus, reactive airway disease	73
3	14 y	Asthma exacerbation	7
4	4 d	Respiratory syncytial virus, status post heart transplant	71
5	2 y	Pneumonia, cystic fibrosis	95
6	15 y	Trauma, acute brain injury	24
7	3 y	Stridor, former 29-week-gestational-age neonate, subglottic stenosis	55
8	1 d	Congenital diaphragmatic hernia	44
9	16 y	Multiple trauma, including chest	48
10	9 mo	Arteriovenous canal	12
11	3 mo	Former 30-week-gestational-age neonate, with bronchopulmonary dysplasia and pulmonary hypertension	95
12	10 y	Liver failure	51
13	3 y	Near-drowning	24
14	10 y	Trauma, lung contusions	96
15	6 y	Multiple trauma, status post-motor-vehicle accident	21
16	4 y	Airway reconstruction, subglottic stenosis	94
17	19 y	Failure of prosthetic tricuspid valve	23
18	9 mo	Reactive airway disease	67
19	7 y	Airway reconstruction, subglottic stenosis	91

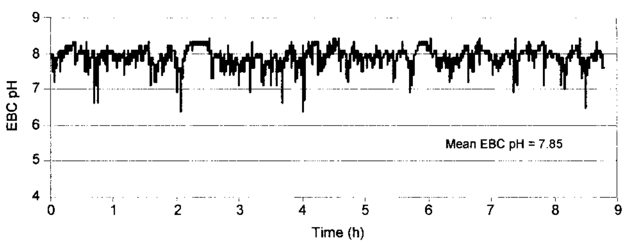

Fig. 4. Condensimetry pH over 9 h, from a 17-year-old victim of a motor-vehicle accident without lung injury or disease. He was intubated (with a cuffed endotracheal tube) for nonpulmonary trauma. The mean pH of the tracing is 7.85, which is a normal exhaled-breath-condensate pH value, compared to large reference ranges of individual exhaled-breath-condensate samples, and is consistent with pulmonary health.

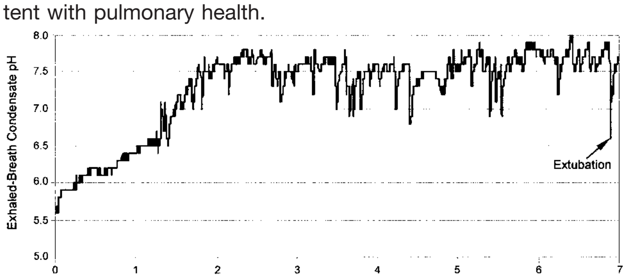

Fig. 5. Condensimetry pH over 7 h, from a 14-year-old female patient intubated with a cuffed endotracheal tube 9 h earlier for status asthmaticus. Note the gradual movement toward pH normalization. The subsequent rapid changes in exhaled-breath condensate (EBC) pH in this patient may reflect acid reflux and aspiration as her sedation was weaned, or, speculatively, it may reflect the occasional opening of individual airways, allowing renewed ventilation of distal acidic airways, which would temporarily and mildly acidify the EBC. This patient was extubated at the 7th hour of EBC pH tracing, with a near-normal EBC pH.

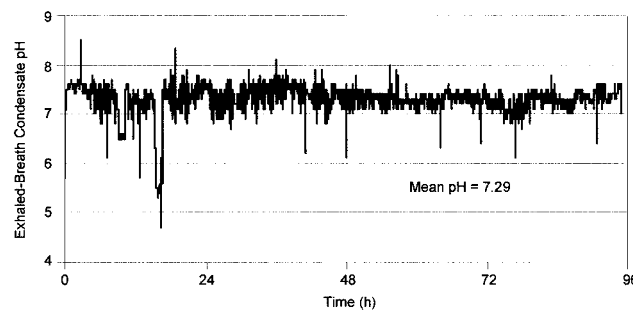

Fig. 6. Condensimetry pH over 96 h from a 2-year-old patient (intubated with an uncuffed endotracheal tube) with cystic fibrosis. The mean pH is 7.29, which is substantially lower than lung-healthy controls. This low baseline pH is consistent with previous reports of exhaled-breath condensate pH from patients with cystic fibrosis and other causes of bronchiectasis.

Figures 4 through 8 show examples of continuous pH condensimetry tracings. These graphs represent up to 57,600 pH measurements from a system that effectively provides a moving average EBC pH as newly collected sample is added to the serial gas-standardizing chambers. EBC pH is measured every 6 s, and the duration of the moving average is determined by the rate of condensate formation; thus, it takes 13–21 min for the condensimeter to register a change in airway pH.

Table 1 summarizes the patients' disease processes. In our series, continuous EBC pH tracings in general revealed gradual changes in EBC pH, including gradual normalization of EBC pH during recovery from acute respiratory distress syndrome and asthma, and gradual

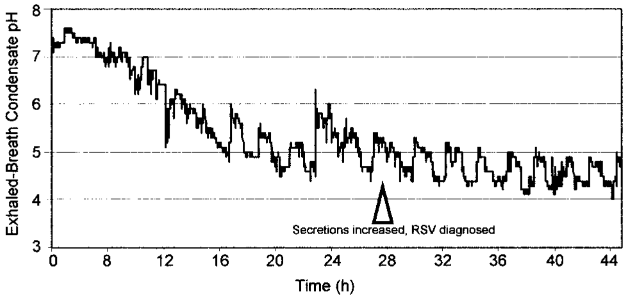

Fig. 7. Condensimetry pH over 44 h, from a 4-year-old patient with tracheal stenosis and evolving respiratory syncytial virus (RSV) infection. This child was intubated with an uncuffed endotracheal tube during tracheal reconstructive surgery 1 week before this tracing was initiated. Continuous condensimetry revealed a gradual and unexpected decline in his exhaled-breath-condensate pH. Eighteen hours after this decline began, he became symptomatic, with pronounced nasal and tracheal secretion production, and was subsequently diagnosed with RSV. This decline in airway pH associated with airway inflammation was evident prior to any clinical indications of deterioration.

acidification of EBC prior to development of symptomatic respiratory-syncytial-virus infection. More rapid changes in EBC pH were seen in patients in whom gastroesophageal reflux with aspiration was expected to be occurring.

In one patient, EBC pH was affected by addition of base to the airway, in the form of tracheally instilled sodium bicarbonate (Figure 9). This patient had cystic fibrosis and was given quarter-strength sodium bicarbonate (8.4%, 84 mg/mL), directly instilled via the ETT, in a clinically indicated effort to thin the mucus. Figure 9 shows movement toward normal pH after the bicarbonate administration at hour 16. In addition, when pH was more alkaline, the EBC pH rose only minimally after bicarbonate administration (data not shown).

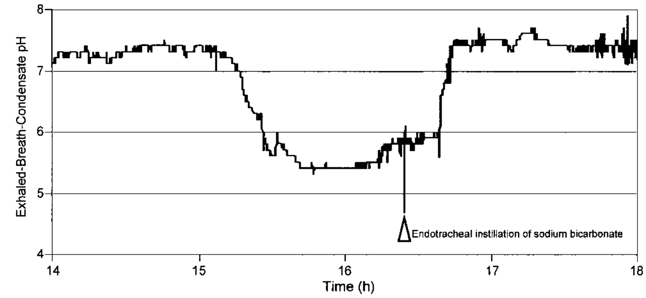

Fig. 9. Effect of tracheal instillation of sodium bicarbonate on exhaled-breath-condensate pH in a 2-year-old patient with cystic fibrosis and profound mucus plugging. Note the reversal of EBC acidification after bicarbonate instillation during hour 16.

Discussion

EBC pH correlates with various indices of airway inflammation,[11] but it may be best to think of EBC pH more directly as an indicator of airway acidification, and acidification as a component of, or precursor to, inflammation. We have begun to consider airway acid stress as a separate but interrelated component of airway disease.

In this project we developed a system to measure and record the gas-standardized pH of EBC collected continuously from the ventilator exhaust port. We tested this system for up to 96 h. EBC pH from patients with prominent lung disease was consistently lower than that from individual samples from lung-healthy intubated subjects in the present study as well as in historical controls published previously.[13] But what can be done when the pH of the airway is found to be low? Although there are case series reporting rapid improvement in airflow obstruction when

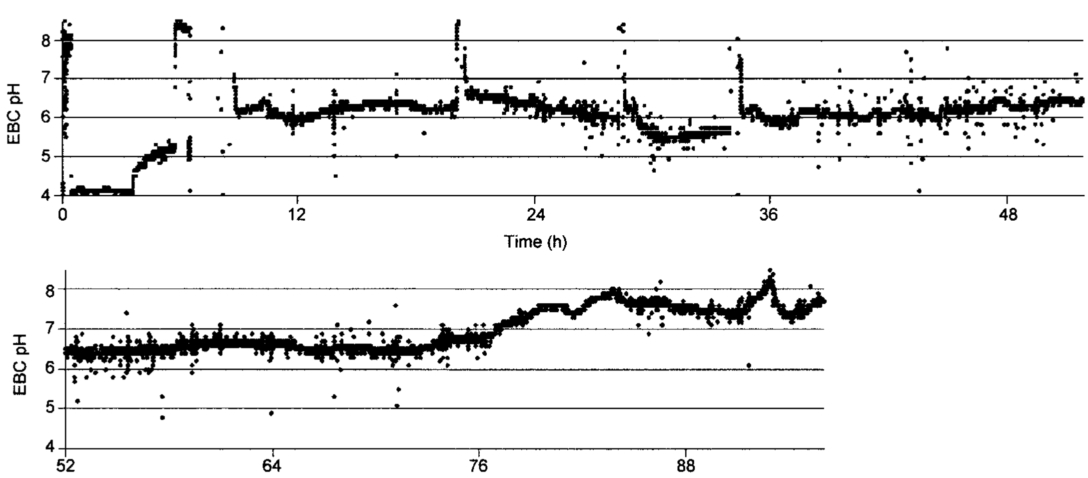

Fig. 8. Condensimetry pH over 96 h, from a 12-year-old female patient (intubated with a cuffed endotracheal tube) with multiple rib fractures and lung contusion from a motor-vehicle accident. By hour 6 the patient had developed acute respiratory distress syndrome (ARDS, ratio of P_{aO_2} to fraction of inspired oxygen < 150 mm Hg). Note that the exhaled-breath-condensate (EBC) pH is initially low, consistent with lung disease, but EBC pH then progresses toward normal. This patient was successfully extubated 24 h after EBC pH normalized.

patients with acute asthma or chlorine-gas-inhalation injury are treated with nebulized bicarbonate,[5,14,15] we do not currently have Food-and-Drug-Administration-approved medications specifically designed to normalize airway pH. As airway pH disturbance is increasingly recognized as an important component of disease pathology, therapeutics will be developed.

Currently, as a diagnostic tool, a low EBC pH strongly suggests that there is an ongoing active pathologic airway or lung process. A low EBC pH can be a key clue to be wary. Identifying precisely *what* is wrong requires some additional thinking on the part of the practitioner. Rapid and transient acidification of EBC probably reflects gastric-acid reflux and aspiration, but, speculatively, may reflect the occasional opening of individual airways, allowing renewed ventilation of distal acidic airways, which could then temporarily and mildly acidify the EBC. Gradual changes in EBC pH more likely reflect primary processes associated with or causing airway acidification, such as evolving infection or exacerbating asthma or chronic obstructive pulmonary disease. Examination of EBC pH patterns may support the use of proton-pump inhibition in certain patients, or lead to earlier diagnostics and therapeutic efforts when a patient's status is deteriorating.

Similar to electrocardiogram electrodes, pH electrodes can suffer from transient electrical interference. These infrequent and very transient downward spikes last for 1–6 measurements (at 6-s intervals) and appear in some of the condensimetry tracings.

If EBC pH is found to be normal in a patient who has just been intubated for an asthma exacerbation, it may be wise to seek other etiologies for the airway obstruction, or to consider earlier extubation. For example, we saw a patient who had an asthma history and was intubated for profound airway obstruction, presumed to be status asthmaticus. However, the EBC pH was high, prompting a more careful evaluation of her chest radiograph, which revealed a mass constricting her airway (subsequently diagnosed as a primitive neuroendodermal tumor).

Instillation of bicarbonate to the airway is likely to be of little benefit when the pH of the secretions is already sufficiently alkaline. However, when the airway is acidic, tracheal bicarbonate may be useful in converting gel-phase mucus plugs at an acidic pH into more fluid sol phase at alkaline pH. Monitoring the airway acidity can provide therapeutic guidance in this setting.

Conclusion

There is increasing evidence that airway pH falls during lung and airway disease, but because most studies have not provided frequent assessments of airway pH, the time course of airway pH changes has not been sufficiently elucidated. We have developed a safe and efficient system of continuously monitoring EBC pH with a conventional ventilator. The enhanced ability to monitor EBC pH during critical illness will improve our understanding of airway pH homeostasis during disease, and provide improved opportunities to evaluate the diagnostic and prognostic utility of EBC pH in the intensive-care setting. It may serve as the lead technology toward the development of a new system of treating airway disease: therapeutic modification of airway pH.

REFERENCES

1. Hunt J. Exhaled breath condensate: an evolving tool for noninvasive evaluation of lung disease. J Allergy Clin Immunol 2002;110(1):28–34.
2. Horvath I, Hunt J, Barnes PJ, Alving K, Antczak A, Baraldi E, et al; ATS/ERS Task Force on Exhaled Breath Condensate. Exhaled breath condensate: methodological recommendations and unresolved questions. Eur Respir J 2005;26(3):523–548.
3. Hunt JF, Erwin E, Palmer L, Vaughan J, Malhotra N, Platts-Mills TAE, Gaston B. Expression and activity of pH-regulatory glutaminase in the human airway epithelium. Am J Respir Crit Care Med 2002;165(1):101–107.
4. Ricciardolo FL, Gaston B, Hunt J. Acid stress in the pathology of asthma. J Allergy Clin Immunol 2004;113(4):610–619.
5. Bosse GM. Nebulized sodium bicarbonate in the treatment of chlorine gas inhalation. J Toxicol Clin Toxicol 1994;32(3):233–241.
6. Jack CI, Calverley PM, Donnelly RJ, Tran J, Russell G, Hind CR, Evans CC. Simultaneous tracheal and oesophageal pH measurements in asthmatic patients with gastro-oesophageal reflux. Thorax 1995; 50(2):201–204.
7. Paget-Brown AO, Ngamtrakulpanit L, Smith A, Bunyan D, Hom S, Nguyen A, Junt JF. Normative data for pH of exhaled breath condensate. Chest 2006;129(2):426–430.
8. Hunt JF, Fang K, Malik R, Snyder A, Malhotra N, Platts-Mills TA, Gaston B. Endogenous airway acidification: implications for asthma pathophysiology. Am J Respir Crit Care Med 2000;161(3 Pt 1):694–699.
9. Tate S, MacGregor G, Davis M, Innes JA, Greening AP. Airways in cystic fibrosis are acidified: detection by exhaled breath condensate. Thorax 2002;57(11):926–929.
10. Gessner C, Hammerschmidt S, Kuhn H, Seyfarth HJ, Sack U, Engelmann L, et al. Exhaled breath condensate acidification in acute lung injury. Respir Med 2003;97(11):1188–1194.
11. Kostikas K, Papatheodorou G, Ganas K, Psathakis K, Panagou P, Loukides S. pH in expired breath condensate of patients with inflammatory airway diseases. Am J Respir Crit Care Med 2002; 165(10):1364–1370.
12. Karnad DR, Mhaisekar DG, Moralwar KV. Respiratory mucus pH in tracheostomized intensive care unit patients: effects of colonization and pneumonia. Crit Care Med 1990;18(7):699–701.
13. Vaughan J, Ngamtrakulpanit L, Pajewski TN, Turner R, Nguyen TA, Smith A, et al. Exhaled breath condensate pH is a robust and reproducible assay of airway acidity. Eur Respir J 2003;22(6):889–894.
14. Douidar SM. Nebulized sodium bicarbonate in acute chlorine inhalation. Pediatr Emerg Care 1997;13(6):406–407.
15. Vinsel PJ. Treatment of acute chlorine gas inhalation with nebulized sodium bicarbonate. J Emerg Med 1990;8(3):327–329.