# Respiratory Care of the Hospitalized Patient With Cystic Fibrosis

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**Hospitalization can occur at any age for patients with cystic fibrosis (CF). The leading cause for admission is an acute worsening of signs and symptoms that can be called a pulmonary exacerbation. The reasons for admission are usually the need for intravenous antibiotics and aggressive airway clearance with good nutritional support. Respiratory therapists (RTs) play a key role in the care of CF patients in the out-patient clinics and taking care of the patients while hospitalized. Following the CF pulmonary guidelines, they administer aerosol delivery and airway clearance while also providing education to patients and families. The RT should have the skills to perform and teach all manners of airway clearance and understand the medications and delivery devices that make up a CF treatment. As CF lung disease progresses, so does the chance that these patients may develop complications such as pneumothorax and hemoptysis, which may require different strategies, especially when airway clearance is performed. The RT needs to have the skills that can take the patient from simple oxygen therapy as lung function deteriorates to the point where chronic oxygen or noninvasive ventilation is needed, or to the point where the end-stage patient waits for a lung transplant. An important aspect of the hospitalization is the interaction between the RT and the patient. To give good therapy is to be a great coach. From infection control to following proper nebulizer protocol, to consistency with airway clearance, to education, the CF RT is there for the life of the patient.** *Key words: respiratory therapist, pulmonary exacerbation, cystic fibrosis, airway clearance techniques, hospital stay, respiratory failure, noninvasive ventilation.* [Respir Care 2009;54(6):769–775. © 2009 Daedalus Enterprises]

## Introduction

Cystic fibrosis (CF) lung disease is one of chronic infection and inflammation. The airways are obstructed with secretions that contain large numbers of bacteria and inflammatory cells, and the natural history of the disease is one of progressive destruction of the airways, with loss of

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lung function and eventual respiratory failure.[1] Patients with CF use a variety of medications and therapies to try to clear their airways of secretions and slow the rate of decline of their lung function.[2,3] However, there are also episodes of worsening signs and symptoms that are commonly referred to as pulmonary exacerbations. Milder exacerbations are often treated in the out-patient setting with oral and/or inhaled antibiotics, but some patients will have more serious signs and symptoms that lead to admission to the hospital for more intensive therapies. These pulmonary exacerbations occur commonly, with at least one exacerbation requiring hospitalization and/or home intravenous therapy occurring in almost 30% of pediatric patients (age $< 18$ y) and in 48% of adult patients in 2007.[4] The following is a review of the role of the respiratory therapist (RT) in the treatment of the hospitalized patient. Although the primary focus of this review is the treatment of the patient with a pulmonary exacerbation, there are other complications that result in the admission of a patient with CF to the hospital, such as a pneumothorax and massive hemoptysis, which are also discussed in Flume,[5] but which will be touched on briefly here as well.

Table 1. Cystic Fibrosis Pulmonary Exacerbation

| |
|---|
| Symptoms |
| Increased frequency, duration, and intensity of cough |
| Increased or new onset of sputum production |
| Change in sputum appearance |
| New-onset or increased hemoptysis |
| Increased shortness of breath and decreased exercise tolerance |
| Decrease in overall wellbeing: increased fatigue, weakness, fever, poor appetite |
| Physical signs |
| Increased work of breathing: intercostal retractions and use of accessory muscles |
| Increased respiratory rate |
| New onset or increased crackles on chest examination |
| Increased air trapping |
| Fever |
| Weight loss |
| Laboratory findings |
| Decrease in $FEV_1$ of $\geq 10\%$, compared to best value in previous 6 months |
| Increased air trapping and/or new infiltrate on chest radiograph |
| Leukocytosis |
| Decreased $S_{aO_2}$ |

$FEV_1$ = forced expiratory volume in the first second
$S_{aO_2}$ = arterial oxygen saturation
(Adapted from Reference 7.)

## What Is a Pulmonary Exacerbation?

Pulmonary exacerbations are events that are best described as a worsening of signs and symptoms of lung infection that warrant more aggressive treatment.[6] Patients may experience an increase in the frequency or severity of their symptoms, such as cough, secretion productions, and dyspnea, or an onset of new symptoms such as hemoptysis, fever, anorexia or weight loss, as shown in Table 1.[7] Clinical signs that may alert the clinician to an exacerbation include changes in chest physical examination and radiological findings, in addition to a decline in spirometry (see Table 1). Many CF care centers are now performing spirometry every clinic visit, looking for changes in lung function. Trending this data, specifically $FEV_1$, can give the care team and the patient/parent a snapshot and a look over time on how the patient is doing, and if treatment needs to be stepped up, as shown in Figure 1. Pulmonary exacerbations can occur at any stage of the disease process and have an adverse impact on quality of life.[8-10] The frequency of exacerbations increases as lung disease worsens, and they are associated with a decline in pulmonary function and earlier mortality.[11-15]

It would seem that making the diagnosis of a pulmonary exacerbation should be relatively straightforward, but, in fact, there is no consensus on specific diagnostic criteria to define an exacerbation. There are a few definitions that have been reported in clinical trials or used in quality initiatives, each with a list of symptoms and signs, with a number of criteria needed to make the diagnosis of an exacerbation.[16,17] Some centers have adopted a pulmonary exacerbation score to improve the consistency with which doctors diagnose and treat a pulmonary exacerbation.[18,19] Some definitions require the presence of a number of clinical criteria and a plan for treatment with parenteral antibiotics.[20] Although this was useful for a clinical trial, it is not helpful in making a diagnosis of an exacerbation in a patient.

The purpose of a definition of an exacerbation is that it should prompt an intervention by the clinician. One attempt at determining a definition used a large database[8] during a period in which 42% of the population was treated with antibiotics for a pulmonary exacerbation. Ten clinical characteristics (increased cough frequency and sputum production, new crackles and wheezing, asthma, symptomatic sinusitis, hemoptysis, weight loss, new acquisition of *Pseudomonas aeruginosa*, and decreased lung function) were studied to identify the 4 characteristics that were most predictive of intervention for pulmonary exacerbation. These characteristics are given in Table 2.[8] The investigators then used the same database to identify all of the patient visits where the patients had at least 3 of the 4 characteristics that would define an exacerbation. Although most events (77% of pulmonary exacerbations) were treated with antibiotics, only 52% of children younger than 6 years who met pulmonary-exacerbation criteria at a clinic visit

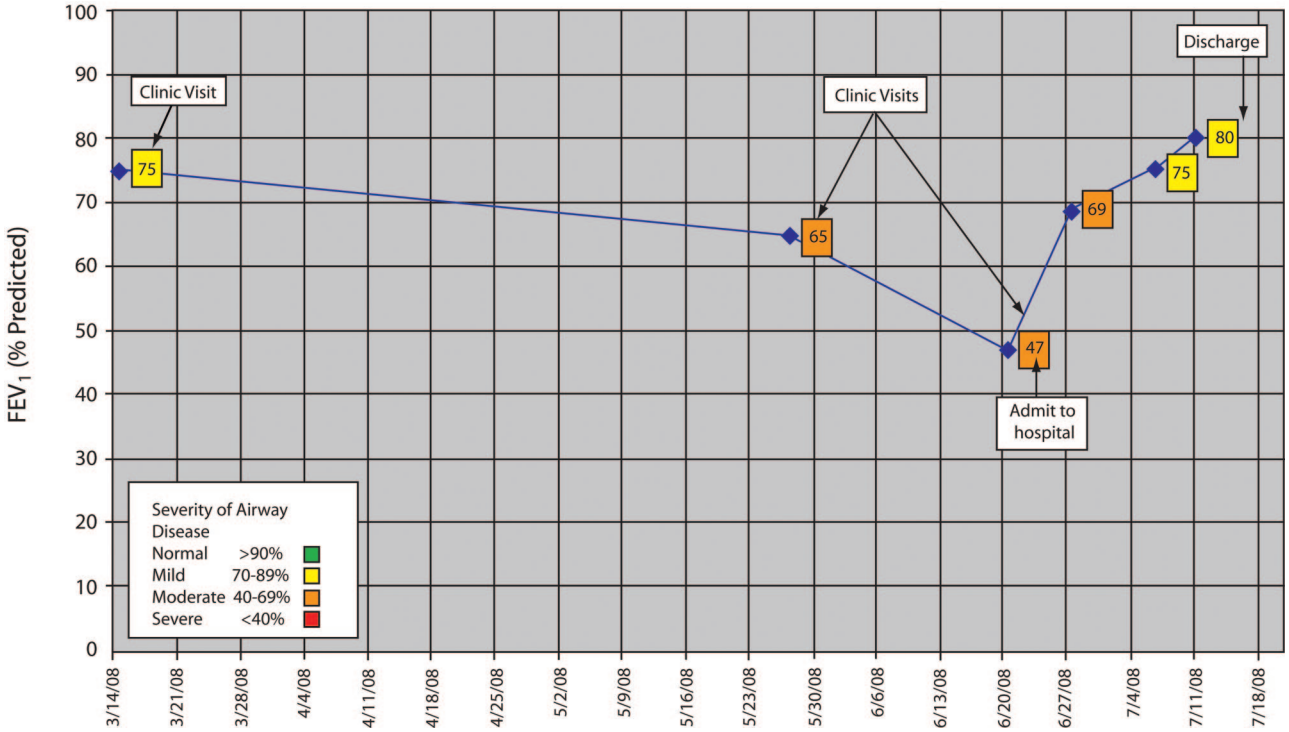


Fig. 1. Percent-of-predicated forced expiratory volume in the first second in a 17-year-old female with cystic fibrosis.

Table 2. The 4 Clinical Characteristics Most Associated With Treatment for Pulmonary Exacerbation in Each Age Group*

| Age Group (y) | | | |
|---|---|---|---|
| < 6 | 6–12 | 13–17 | > 18 |
| New crackles | Decline in $FEV_1$ (% predicted) | Decline in $FEV_1$ (% predicted) | Decline in $FEV_1$ (% predicted) |
| Increased cough | Increased cough | Increased cough | New crackles |
| Decline in weight-for-age percentile | New crackles | New crackles | Hemoptysis |
| Increased sputum | New *Pseudomonas aeruginosa* | Hemoptysis | Increased cough |

* From stepwise multiple regression analysis. Evaluable number of patients included: 2,116 of 2,448 (< 6 y), 1,175 of 3,807 (6–12 y), 1,241 of 2,170 (13–17 y), and 1,606 of 3,267 (> 18 y).
$FEV_1$ = expiratory volume in the first second
Data from Reference 8.

were treated with antibiotics. This suggests that the definition is either still too sensitive or that clinicians are under-treating exacerbations.

### How Is an Exacerbation Treated?

The patient who is admitted to the hospital for treatment of an exacerbation is likely to be treated with intravenous antibiotics. These have been shown to be an effective component of the treatment of a pulmonary exacerbation.[21] However, there are a number of other therapies that are provided to the patient in addition to antibiotics, including airway-clearance therapies (ACTs) and nutritional support. The CF pulmonary guidelines on the management of pulmonary exacerbations will recommend that medications used chronically for maintenance of lung health and ACTs be performed as part of the treatment of an exacerbation of pulmonary disease.[2]

The admission of a patient for treatment of a pulmonary exacerbation requires a comprehensive treatment plan with interaction of multiple disciplines, including physicians, nursing, pharmacy, dietary, respiratory therapy, and physical therapy. For the child there may also be school lessons and play activities through child life services provided by the hospital. All of these work together in order to provide optimal care in an efficient manner and still let the patient get some rest.

### The Role for the Respiratory Therapist

The CF patient admitted for treatment of a pulmonary exacerbation may need many, or even all, of the services typically provided by an RT. Bedside care may include the administration of aerosolized medications (eg, antibiotics, dornase alfa, bronchodilators, hypertonic saline), performance of ACTs, provision of supplemental oxygen, initiation and management of noninvasive and invasive mechanical ventilatory support, as well as psychosocial support. During the hospitalization, RTs may perform pulmonary function testing to help gauge the patient's baseline lung function upon admission. RTs may also repeat pulmonary function tests during the hospital stay to measure improvement and provide physicians with information that can aid in their patient assessment. Some hospitals also have the ability to do *infant* pulmonary function. In some tertiary-care centers RTs are utilized to assist with bronchoscopies.

### Anatomy of the Hospital Stay

The patient with CF will be admitted to a private room with aerosol droplet precautions, consistent with infection-control practices recommended by the CF Foundation,[22,23] The physician orders will typically include the same aerosolized medications that are recommended for chronic therapy in this population.[2] Of note, there have been few studies and no consensus regarding the sequence of delivery of inhaled medications, or *when* during that sequence to conduct ACTs. One intuitive approach that makes sense, as mentioned by Flume et al,[2] is to first deliver the $\beta$-agonist aerosol to open the distal airways, then deliver hypertonic saline[24] to hydrate the airways and improve ciliary transport, then follow with dornase alfa[20] (rhDNase) to break down the thick tenacious secretions. Finally, perform airway clearance to remove the secretions, and then conclude with aerosolized antibiotics delivered to the "clean" lungs. Of interest are 2 papers by Dasgupta and colleagues,[25,26] studying the effect of airway oscillations on CF secretions when combined with rhDNase, done in vitro. The first study[25] was done with high-frequency chest compression, while the second study[26] used the Flutter device. The authors suggest that combining rhDNase with mechanical oscillation can decrease "spinnability" of secretions and may have a better therapeutic potential for secretion clearance in CF lung disease.

Although some medications may be provided by metered-dose inhaler or dry-powder inhaler, those administered by nebulization may require a specific nebulizer for use. Most hospitals will have a preferred nebulizer brand for routine treatments, but there are some nebulizers that are better suited to deliver specific medications such as antibiotics.[27,28] The recommendations for the use of a specific nebulizer brand with inhaled medication can be found in that drug's package insert. Some hospitals may view the durable nebulizers recommended for use with medications such as tobramycin solution for inhalation as cost-prohibitive. However, given the challenges of endobronchial aerosol drug delivery, it is probably best for most departments to comply with the manufacturer's recommended delivery device. A substitute delivery system could be employed only where there are compelling data showing that it is technically and clinically comparable to the recommended device with respect to inhaled mass and particle size distribution. The RT is typically responsible for proper cleaning of these devices after patient use in the hospital and may also teach these techniques to the patient and family. The CF Foundation recommends disinfection, sterile water rinse, and air drying for each nebulizer after each treatment that is given.[22,23,29] Adherence to disinfection guidelines will reinforce behaviors the patient and family should mirror upon discharge. Most hospitals don't have an area designated for the cleaning of nebulizers or the ability to keep cleaning supplies in the patient's room. One alternative is to change the nebulizer after every treatment, but this too can be cost-prohibitive. Some hospitals will eliminate the disinfection after every treatment, and will instead shake out the remaining solution, then air dry after each treatment, and discard the nebulizer every 24 hours.[30] Nebulizers should be allowed to dry away from the sink on a clean paper towel or cloth to avoid contamination.

### Airway-Clearance Therapies

As stated earlier, the CF pulmonary guidelines for treatment of pulmonary exacerbation will recommend continuing ACT. Those therapies may need to be stepped up or intensified during the hospital stay. There are a number of therapies available: breathing techniques such as autogenic drainage and active cycle of breathing; the use of manual therapy such as postural drainage and percussion; or the use of mechanical devices, including high-frequency chest-wall oscillation, positive expiratory pressure (PEP), and oscillatory PEP.[3] When patients with CF are hospitalized, the RT can begin with the ACT regimen the patient was using at home, when appropriate. Therefore, it is imperative that the hospital staff be knowledgeable in all of the possible therapies that can be employed. This includes the ACTs typically performed at the hospital, in addition to techniques that may not be commonly used in acute-care facilities but performed by patients at home.[31,32] The CF patients we treat in the hospital can range in age from newborn infants to adults. It is still common practice to initiate airway clearance at diagnosis. Most centers in North America still perform chest physiotherapy or postural drainage, percussion, and vibration on infants. But some com-

pelling evidence from Button and colleagues in Australia[33-35] has shown that placing these infants in the head-down position may result in an increase in gastroesophageal reflux. Button and colleagues also found evidence of substantial symptomatic and silent reflux in the pre- and post-lung-transplant patients.[36] Besides gastroesophageal reflux, oxygen desaturation in the moderate-to-severe patient has been reported.[37] Manual therapy is very labor-intensive, requiring anywhere from 15 min to 30 min to complete, and there is a lack of evidence for its effectiveness, as reported by van der Schans.[38] Since the mid-to-late 1980s, hospitals have slowly moved away from chest physiotherapy and moved to other forms of airway clearance. All these newer forms require the patient to actively participate in their treatment. RTs can use this time to coach the patient to get the most effective treatment. Since airway clearance is intensified during hospitalization for exacerbations, a combination of airway modalities may be used. This may provide a unique opportunity for the RT to introduce the patient to new ACTs.

Educating patients and families on the proper ACT performance is important for effective therapy. Not only does this offer greater immediate benefit, but also helps the patient to perform the prescribed therapy after discharge from the hospital. It is important to assess the patient's and family's educational needs. Some patients may require intensive education, while others may have decades of experience.

In order to have the most effective treatment of CF patients, CF centers have advocated that acute-care facilities have a designated staff of RTs to work with CF patients. Commitment to a core group of RTs dedicated to caring for CF patients facilitates staff education and competency assessment. It also provides greater continuity of care for hospitalized CF patients.

## Special Considerations

### Acute Complications of Cystic Fibrosis

Patients with CF may suffer other complications that result in admission to the hospital, including pneumothorax and hemoptysis, which Flume discussed in greater detail.[5] Some clinicians may be reluctant to provide ACT for patients with these conditions, for fear it will exacerbate the problem (eg, break free a clot in hemoptysis). Also, patients with pneumothorax are likely to be treated with a chest tube that can cause considerable pain, and ACT may aggravate that pain. However, it is the underlying infection and inflammation that have contributed to these complications, and if the patient stops performing ACT, there is great risk for worsening of airways disease.

Therefore, ACT can be continued in the patient with CF who is admitted to the hospital with these complications, but with some notable cautions. For example, when using ACT for a patient with pneumothorax, the active cycle of breathing or autogenic drainage can be used. These avoid the use of positive pressure and reduce the likelihood of strong paroxysmal coughing that may make the pneumothorax worse. For the patient with hemoptysis, PEP is a good choice, as it promotes stabilization of the airway without the vibrations that other techniques may cause.

**Respiratory Failure.** This complication is also discussed elsewhere.[5] The RT may be asked to assist the patient with supplemental oxygen and noninvasive ventilation. Patients with CF can become hypoxic during a pulmonary exacerbation. Initial treatment may be with a nasal cannula with humidification.[39-41] The RT should be aware that the patient has sinus disease,[42] as a nasal cannula may not be the best option, and an air-entrainment mask may be preferable.

For patients with mild-to-moderate-stage lung disease, acute respiratory failure is thought to be reversible, and intubation with mechanical ventilation is appropriate. For the patient with advanced-stage disease, intubation and mechanical ventilation are not recommended.[43] Rather, patients may be treated with noninvasive ventilation, with air that has been warmed and humidified.[44-49] The intent of noninvasive ventilation is to relieve acute dyspnea, but also to relieve other symptoms of chronic respiratory failure, such as morning headaches, exertional dyspnea, daytime lethargy,[44,50] and peripheral edema.[47] Noninvasive ventilation and short-term conventional ventilation have been used as a bridge to lung transplantation.[50-56]

## Discharge From the Hospital

There are no studies that have determined the proper duration of antibiotic therapy for CF pulmonary exacerbation. Some patients will improve during the hospital stay and may be discharged home to complete the intravenous antibiotics. The average duration of intravenous antibiotics for treatment of an exacerbation is 14–15 days.[4] The clinician may begin a course of therapy with the plan for approximately 2 weeks of therapy, but ultimately will stop the antibiotics when the patient has improved clinically—that is, when the symptoms that led to the admission have resolved and/or when pulmonary function testing has improved to the prior baseline. When the patient is being discharged, whether there will be a continuance of intravenous antibiotics or not, the patient and family should be ready and able to continue all other aspects of the treatment regimen.

## Summary

Hospitalization is a common occurrence for the patient with CF, primarily to address acute complications associated with the chronic airways infection. There may be other indications for admission that were not addressed here (eg, sinus surgery, nutritional support), but the basic principles for chronic CF management are the same and will involve the RT. The RT should be knowledgeable about CF and the aerosol medications for this indication, and skilled with the various methods of ACT. But one of the most important skills the RT should possess is being a good coach and an educator of the patient, and sometimes the patient's family members. Although not discussed here, the time the RT spends with the patient and family members builds a strong psychosocial relationship that will benefit the patient as much as the RT's technical acumen.

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## Discussion

**Flume:** With respect to the guidelines on treatment of CF pulmonary exacerbation, we specifically mentioned continuing chronic medications and airway clearance, because many of the published studies did not discontinue the therapies. In fact, many of the airway-clearance studies were entirely in-patient studies, so we didn't find any compelling reasons to change the recommendations. A caveat to that, though, and my first question is, what do you do about TOBI [tobramycin solution for inhalation] in the setting of intravenous tobramycin?

**Newton:** In our hospital we usually stop TOBI with patients who are on it at home, primarily because they are placed on intravenous tobramycin and a second intravenous antibiotic.

**Flume:** We don't know if it should be continued, because there are no data on efficacy.

**Newton:** True.

**Flume:** But there is a question of safety, and the same can be said for ibuprofen in the setting of intravenous tobramycin.

With respect to airway clearance, our approach is to ask the RT to serve as a consultant. The physician does not prescribe a specific airway-clearance therapy; instead, they request "airway clearance." The expectation is that the RTs will find out what airway-clearance therapy the patient prefers, and start with that therapy. As the hospitalization goes on, the RT asks about introducing other

therapies and assesses the patient's skill in performing those therapies. It's a good opportunity to introduce therapies to patients.

However, not all RTs are skilled at this role, and we have to be cautious about how we recommend a strategy. As an example, I admitted a patient and I said that I wanted the patient to be introduced to both IPV [intrapulmonary percussive ventilation] and vest therapy, but I later discovered that the patient was receiving those therapies simultaneously, which seemed awfully uncomfortable.

**Newton:** We've had similar miscommunication problems. I put a patient who had very floppy airways and was doing poorly on vest therapy, and I added low-level PEP during vest therapy, and it worked really well. I've done this for a couple of patients with floppy airways. I had an order from the attending pulmonologist stating the concurrent vest/PEP treatment. To the next shift RT I described it in detail and wrote it down, but a couple of days later I found they were doing the PEP treatment, *then* the vest therapy, which is completely wrong.

**Flume:** No studies have determined the proper duration of antibiotics. We looked at the CF Foundation patient registry to determine the average duration, and the range was 3 to 33 days. There was a small peak at around 16 days. But it was not consistent.

**Newton:** You are correct. I think our average is 14 days, and I got the same sense in the reading I did.

**Lester:** At the time a patient is admitted to the hospital is when we really want to deliver these medications properly, and there's this huge discrepancy about what kind of nebulizers people use in the hospital. Sometimes it's an administrative decision, but it can be influenced by the pulmonologists in charge. With the Pari LC Plus, do you dispose of them every day?

**Newton:** Yes. We use the Pari LC Plus and we use new ones every day.

**Lester:** Those are expensive. We use the Pari LCD for TOBI and Pulmozyme in the hospital, and dispose of them in the hospital. They're about 99 cents apiece.

**Newton:** Our institution decided to go with the manufacturer's recommendation, that the only nebulizer approved to deliver TOBI is the Pari LC Plus.

**Geller:** This is an issue that people talk about a lot, but I think if you look at Kesser's presentation carefully, you'll realize that most of the variability in drug delivery is patient-based, not device-based. You can have a 2-fold or even 4-fold difference in drug delivery with different devices, but you can have a 1,000-fold difference in pharmacokinetics and pharmacodynamics in one patient versus another, so the variability is patient-derived.

I think it's most important for the RT to be in the room and to coach the patient to inhale deeply and slowly, whatever nebulizer they're using, so at least some of the dose gets there. I can't tell you how many times I've seen patients using the "Clinton technique"—"I didn't inhale"—with the nebulizer hanging outside their mouth, on a vest, not taking deep breaths, and so forth. They need to be coached; it's an individual patient issue, and not so much a nebulizer issue. You can deliver a lot of drugs with cheap nebulizers in the hospital, realizing that a lot of them aren't going to get the job done, but most of them will, so coaching is probably more important.

**Newton:** I couldn't agree more. And we need to get away from the practice of giving blow-by treatments to our smaller patients.

**Geller:** And whether or not it's air-driven, oxygen-driven, or compressor-driven, those are all important things in general over time, but for the acute setting in the hospital at 50 psi, all that does is guarantees that you're going to get the flow rate you've set on the flow meter. With a compressor at home there is no guarantee of flow rate.

**Newton:** Correct. That's a whole other topic in itself.