The Adult Cystic Fibrosis Inpatient Resource Manual

A guide for patients, families, and hospital staff

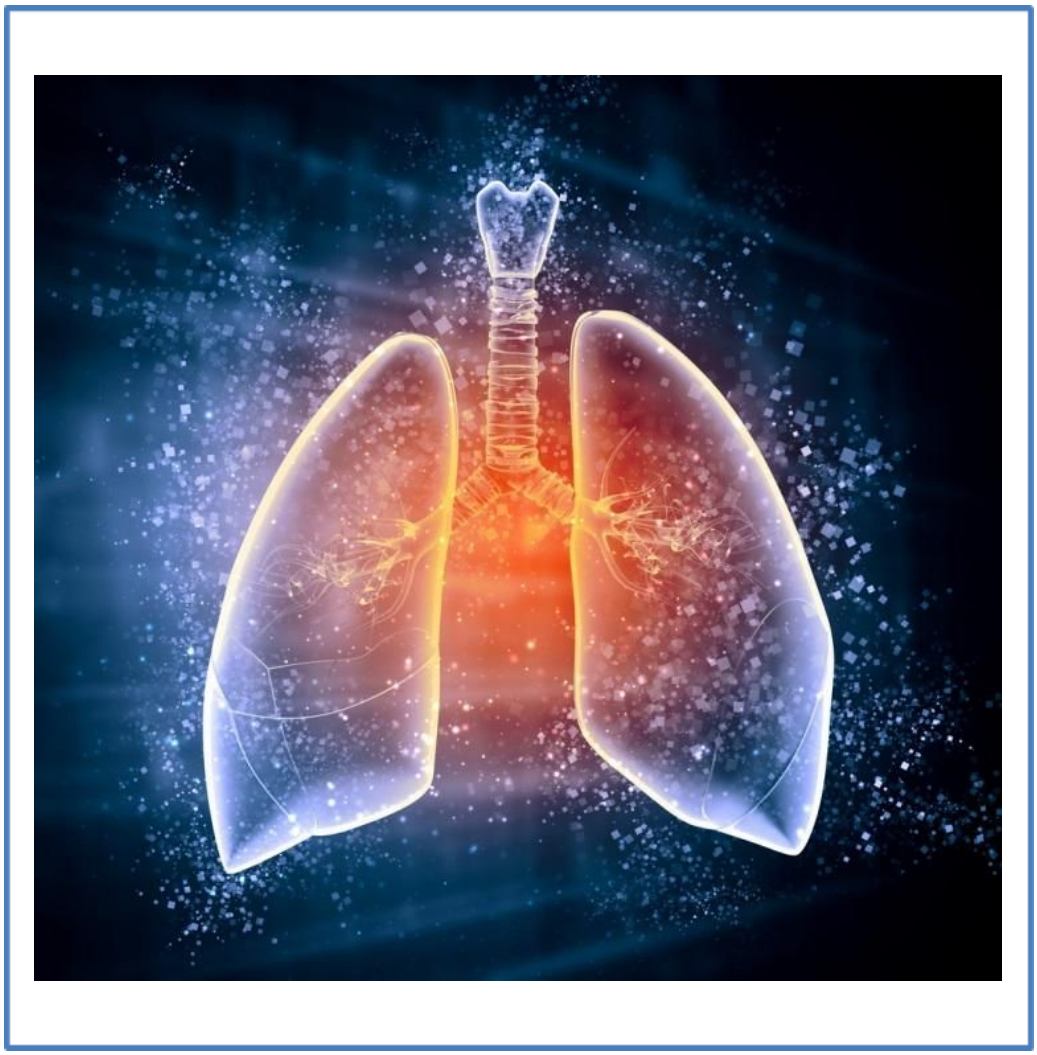

Image from: https://cdn.bronchiectasisnewstoday.com/wpcontent/uploads/2015/05/shutterstock_134672633.jpg

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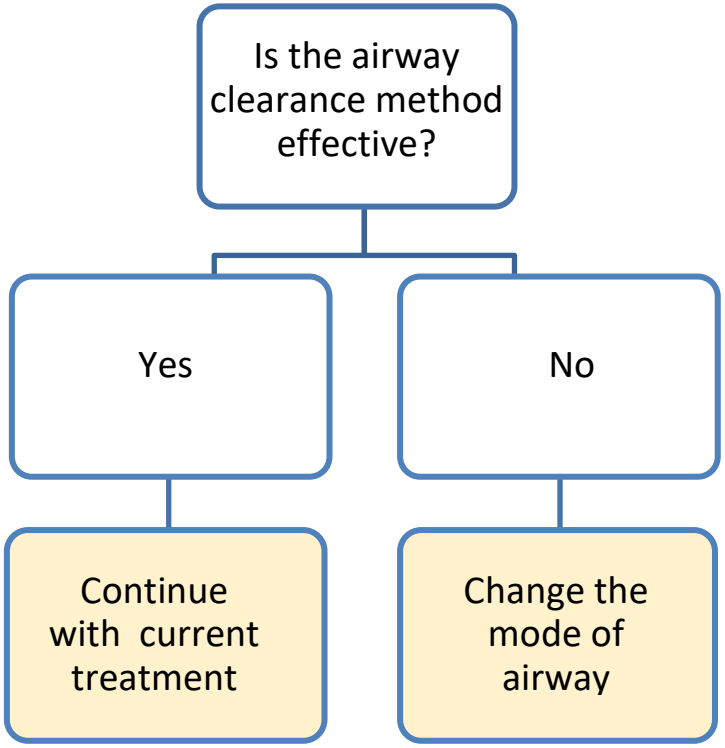
Introduction

Welcome to the Inpatient CF Service at Maine Medical Center (MMC). Admissions can be a stressful and challenging time. This guide is meant to provide general information about the care of CF. It also gives an overview of the various people, services, and resources that are available to CF patients during their admissions to MMC, as well as lay out expectations and guidelines. This guide is meant to be a resource for patients, families, nurses, physicians and advanced practice providers. This is not an exhaustive text but is a living resource that also contains some web links for additional video content, detailed information and consensus documents that you may wish to explore after getting an overview. Please read through this guide and let us know if you have questions or concerns. Suggestions for how to improve this resource and the inpatient experience at MMC are always welcome.

General Airway Clearance Decision Tree



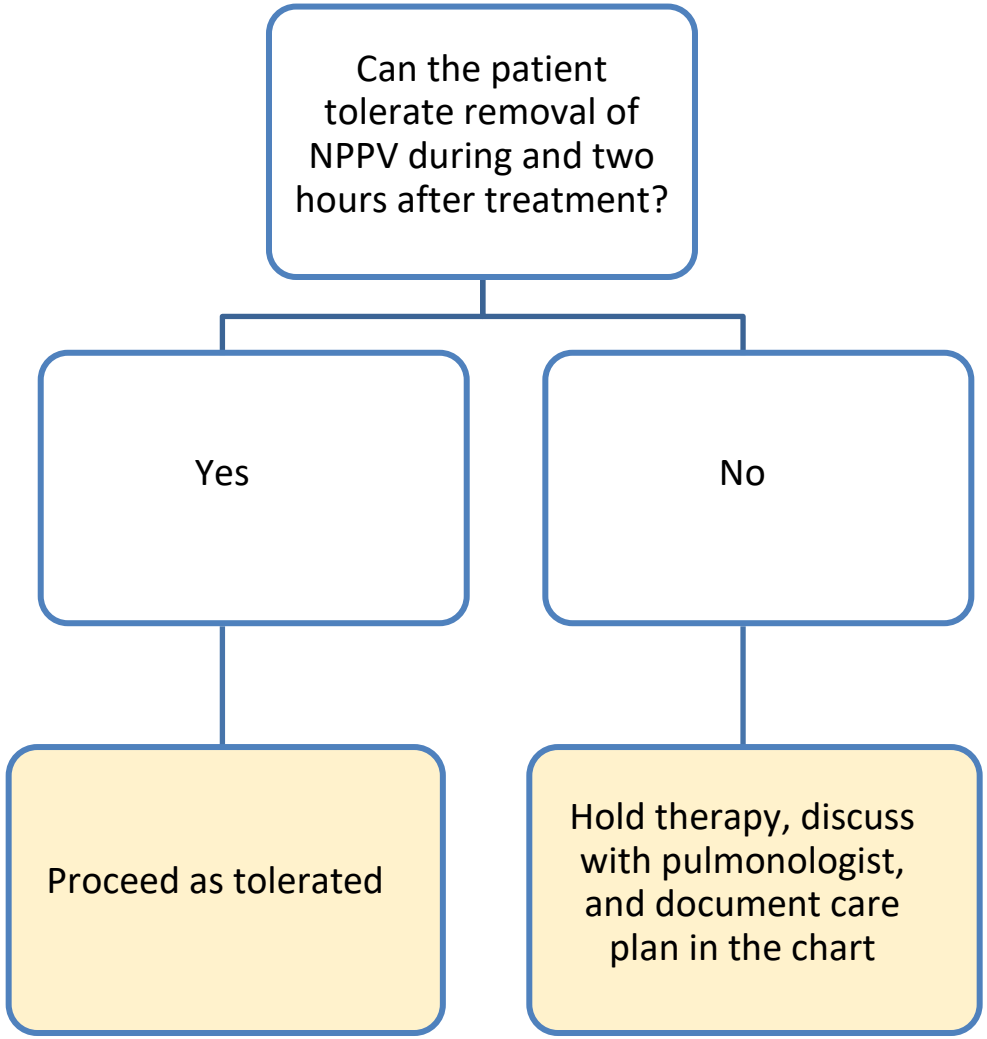
Signs that treatment is effective:

- Productive cough during and up to 2 hours following treatment
- Improved air movement
- Improved airflow on spirometry
- Improved reported sense of well-being and chest congestion
- Resolution of leukocytosis and/or fever

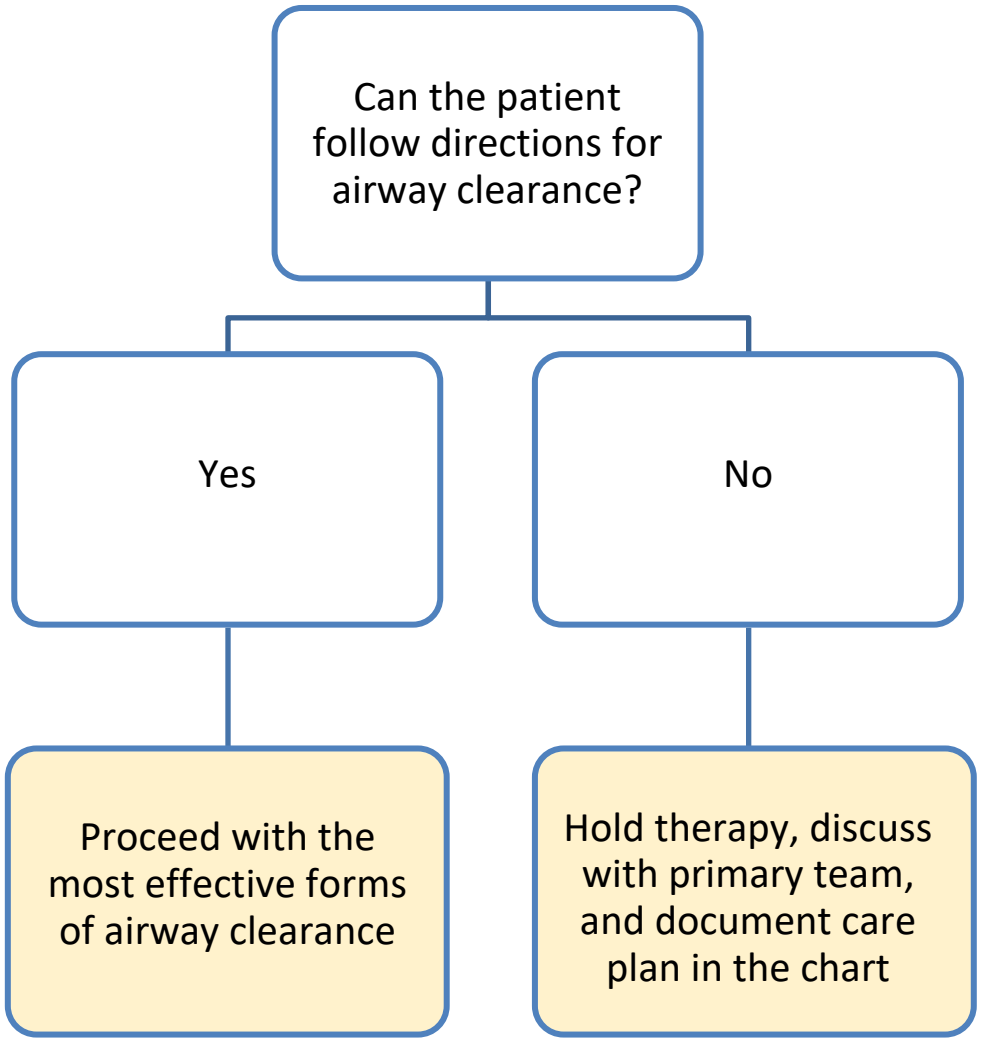
- Airway Clearance Technique (ACT)
- Percussion
- Postural Drainage
- Vibration
- Shaking
- High Frequency Chest Wall Oscillation (for example, “Vest”)
- Active Cycle Breathing Technique
- Positive Expiratory Pressure Device (for example, “Aerobika”)
- Autogenic Drainage
- Exercise

Modes of Airway Clearance:

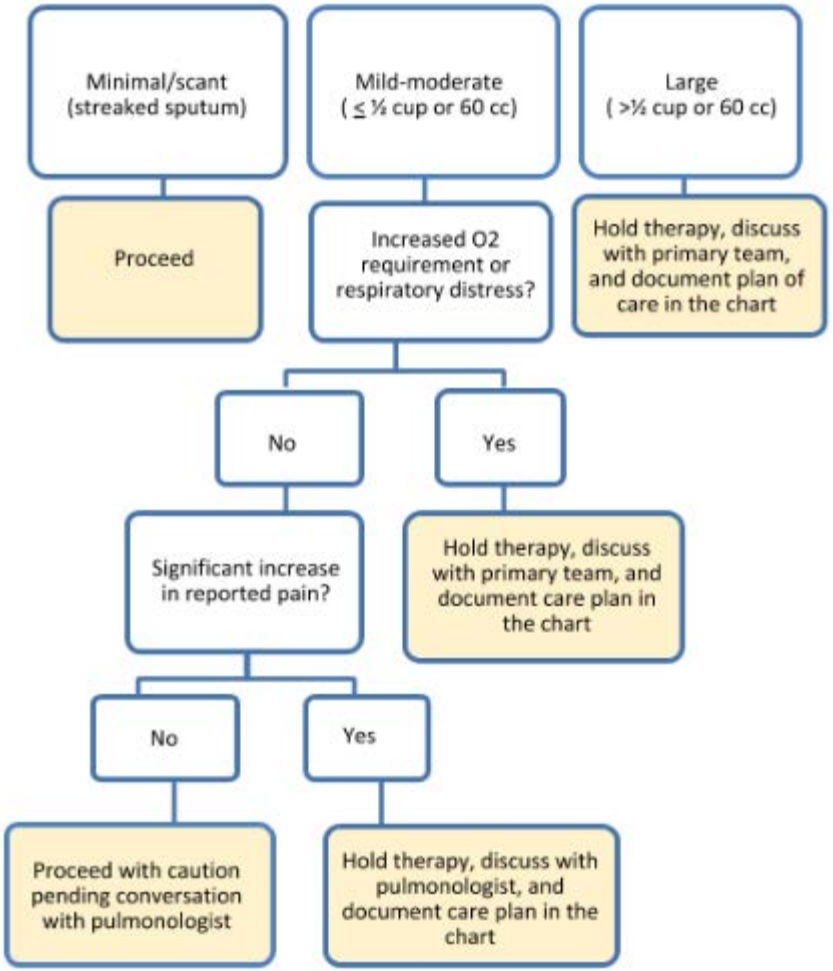
Non-invasive Positive Pressure Ventilation and Airway Clearance Decision Tree



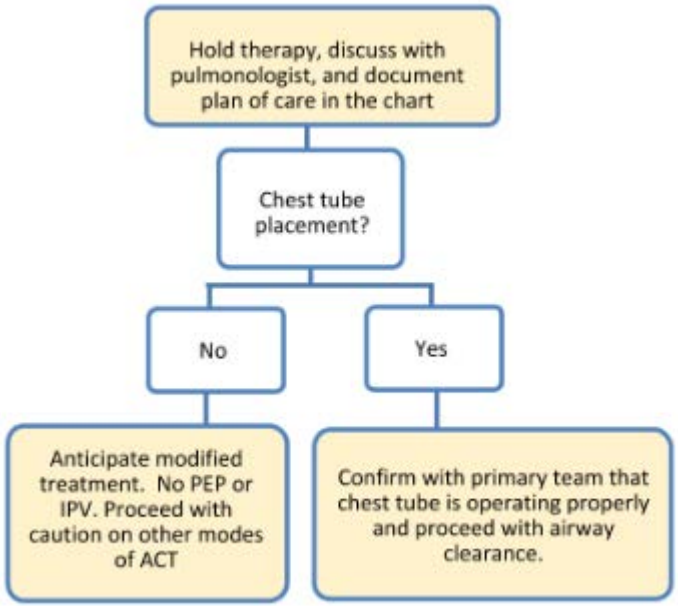
Airway Clearance and Cognition Decision Making Tree



Airway Clearance and Hemoptysis Decision Tree



Airway Clearance and Pneumothorax Decision Tree



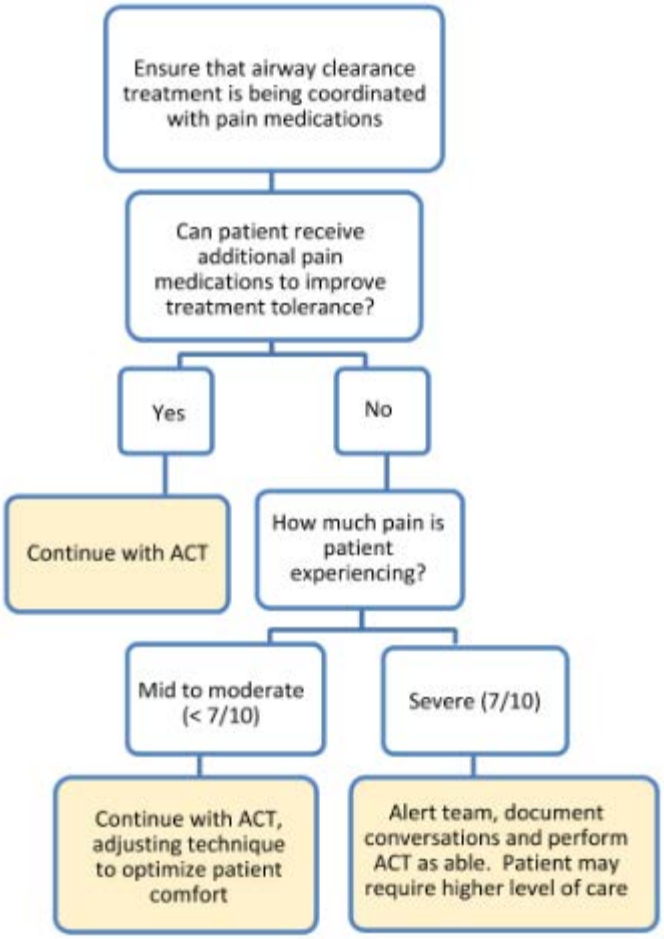
Small & Large pneumothorax:

- No lifting weights until 2 weeks after it has resolved
- No BiPAP

Large pneumothorax:

- No vigorous aerobic activity for 2 weeks after it has resolved

Pain and Airway Clearance Decision Making Tree


Ensure that airway clearance treatment is being coordinated with pain medications
Can patient receive additional pain medications to improve treatment tolerance?
Yes
No
Continue with ACT
How much pain is patient experiencing?
Mid to moderate (< 7/10)
Severe (7/10)
Continue with ACT, adjusting technique to optimize patient comfort
Alert team, document conversations and perform ACT as able. Patient may require higher level of care

The Adult Team and Contacts

	Name	Phone	Pager
Program Director	*Jonathan Zuckerman*	*776-8969*	*741-7761*
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Social Worker	*Simon Macdonald*	*662-1093*	*662-1093*
Social Worker	*Meg Hall*	*662-5522*	
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History & Background

HISTORICAL PERSPECTIVE

Cystic fibrosis (CF) was first described in the medical literature in the 1930's. In the early part of the century children frequently died in infancy due to failure to thrive and intestinal obstruction. The importance of pulmonary disease in cystic fibrosis was therefore not emphasized in early accounts of the disease. The term "mucoviscidosis" was ascribed to a condition characterized by plugging of organ passages throughout the body with viscous secretions. At autopsy the architecture of the pancreas was noted to be deformed by secretion-filled sacs and scars, giving rise to the term "cystic fibrosis of the pancreas". Mothers of affected children reported to physicians that the infant skin had a distinctly salty taste when kissed. During an extreme heat wave in 1949 in New York City Paul di Sant'Agnese discovered a remarkably high sweat salt concentration from a number of infants brought to Babies Hospital. These astute observations led to the development of a diagnostic test for the disease in the 1950's which remains standard to this day—the sweat chloride test. With the recognition and management of the gastrointestinal manifestations of CF in early childhood and the advent of pancreatic enzyme replacement therapy, we now see that progressive pulmonary embarrassment is the primary cause of morbidity and mortality in these patients. Tremendous strides have been taken over the past 50 years to improve the length and quality of life for patients with CF. As recently as the 1960's an average child born with CF was not expected to live beyond the teen years. Today the median life expectancy of patients with CF is over 40 years.

THE CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (THE CFTR)

Prior to the cloning of the gene responsible for cystic fibrosis, scientists knew that the disease was associated with abnormal transport of salt and water across epithelia. Investigators at the University of North Carolina found that the basal level of sodium absorption across CF respiratory epithelial cells was increased and chloride transport was reduced compared to normal. In addition CF epithelial cells, unlike normal cells, did not demonstrate increased chloride permeability after cAMP stimulation. These curious results led to the hypothesis that airway secretions in CF become dehydrated, impairing mucociliary clearance. The hypothesis further predicts that the airway becomes colonized with pathogenic organisms, inciting the vicious cycle of lung destruction. When the gene was first cloned in 1989 and localized to chromosome 7, it was unclear whether the protein product would be an ion transporter or a protein regulator of epithelial ion transport; hence the cumbersome name "cystic fibrosis transmembrane conductance regulator (CFTR)". CFTR was subsequently shown to be a cAMP activated chloride channel. However, its designation as a membrane conductance regulator remains appropriate, as it appears to regulate the activity of other ion channels, such as the epithelial sodium channel

and the outwardly rectifying chloride channel. The full repertoire of functions of the CFTR protein remains to be elucidated, and investigators are still trying to develop a unifying explanation for the association of altered epithelial ion transport and progressive respiratory tract infection.

DIAGNOSIS

The diagnosis of CF is usually made on clinical grounds, frequently on the basis of the classic triad of pulmonary disease, pancreatic insufficiency and an abnormally high sweat chloride concentration >60 mEq/L. In recent years it has become increasingly recognized that patients with CF may present with subtle abnormalities. Such patients with mild phenotypes may not seek medical attention until adulthood and may have little, if any, overt sinopulmonary symptoms. It is therefore important for the internist or adult pulmonologist to consider CF in the differential diagnosis of conditions as varied as recurrent sinusitis, portal hypertension, male infertility, idiopathic recurrent pancreatitis and bronchiectasis. The sweat chloride test remains the standard laboratory test for establishing the diagnosis. The test should only be performed in a certified laboratory where two tests of satisfactory sweat weight can be consistently obtained. Up to 4% of normal adults will have a sweat chloride concentration >60 mEq/L. Furthermore, a significant number of CF patients will have sweat chlorides between 40-60 mEq/L –in the "gray zone" (though less than 0.5% will have a value <40 mEq/L). In these cases genotype analysis may prove diagnostic.

GENETICS/CARRIER SCREENING

CF is the most common fatal genetic disease in the Caucasian population, affecting between 1:2500-3000 live births. Since CF is inherited as an autosomal recessive condition, this puts the carrier rate at about 1 in 25-30 in persons of Northern European descent. The most common CF mutation is a 3 base pair deletion in exon 10 which results in a deletion of phenylalanine from position 508 of the CFTR protein (F508). At least one F508del mutation is found in approximately 90% of CF patients. However, over 1600 mutations, many of very low frequency, have been identified in the gene. All states now routinely screen newborns for CF. Newborn screening and early intervention with nutritional therapies provides distinct benefits including improved height, weight and cognitive function. These therapies also may impact respiratory function and life expectancy, and reduce hospitalizations.

CLINICAL MANIFESTATIONS

Classic CF presents as progressive suppurative sinopulmonary disease associated with pancreatic insufficiency. However, other organs with epithelial cell linings are also affected. These organs include the sweat gland and duct, pancreas, gastrointestinal tract, biliary tree, and reproductive tract. Pulmonary disease accounts for over 85% of the mortality attributable to CF and typically

results in an average annual decline in the FEV_1 of 1-2% in adult patients. The radiographic hallmark of CF is upper lung zone predominant cystic bronchiectasis. A number of important problems commonly challenge these patients, including the following, based on annual figures from the 2015 CF Patient Registry:

1) Hemoptysis: massive in 1.8%.
2) Pneumothorax requiring chest tube: 0.8%
3) Allergic bronchopulmonary aspergillosis: 7.7%
4) Cirrhosis: 1-3%
5) Distal intestinal obstruction syndrome (DIOS): 5.9%
6) Sinusitis: 49.2%
7) Reactive airway disease: 31.7%
8) Osteopenia: 21.5%
9) Diabetes mellitus: 34.9%
10) Biliary cirrhosis with or without portal hypertension: about 3.1%
11) Arthritis and arthropathy: 5.9%

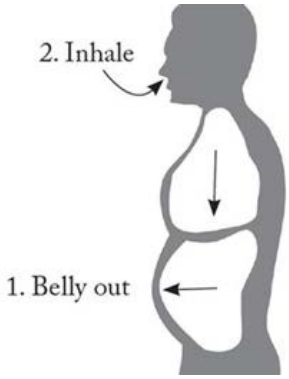
Airway Clearance-Active Cycle Breathing

The Active Cycle Breathing Technique (ACBT) has 3 essential components:

1. Breathing control or relaxed breathing
2. Thoracic expansion exercises
3. Forced expiratory technique with “huff coughing” (see section on this technique)

BREATHING CONTROL

Gentle breathing using the diaphragm. The patient should be relaxed and breath at normal tidal volumes (see Figure). On inspiration the patient should concentrate on having the diaphragm “drop” so that air can enter and fill the lungs “from the bottom up”, much like filling a glass with water. This is done for 3-4 breaths.



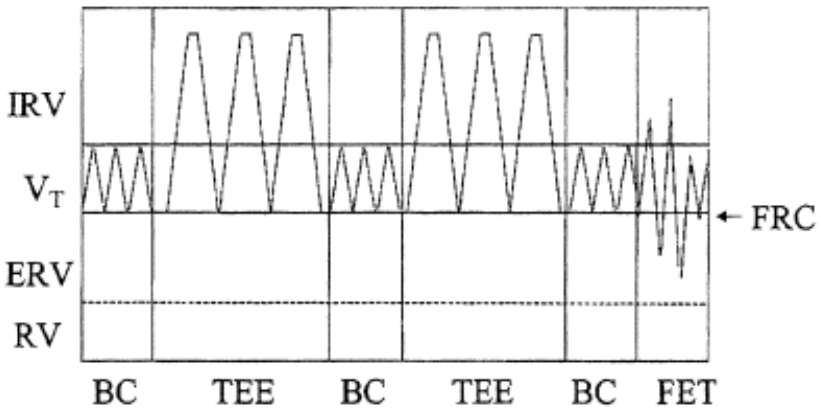
Cartoon of breathing control (http://www.kliniknoridah.com/wp-content/uploads/2017/05/breathing-physiotherapy.jpg)

THORACIC EXPANSION EXERCISE

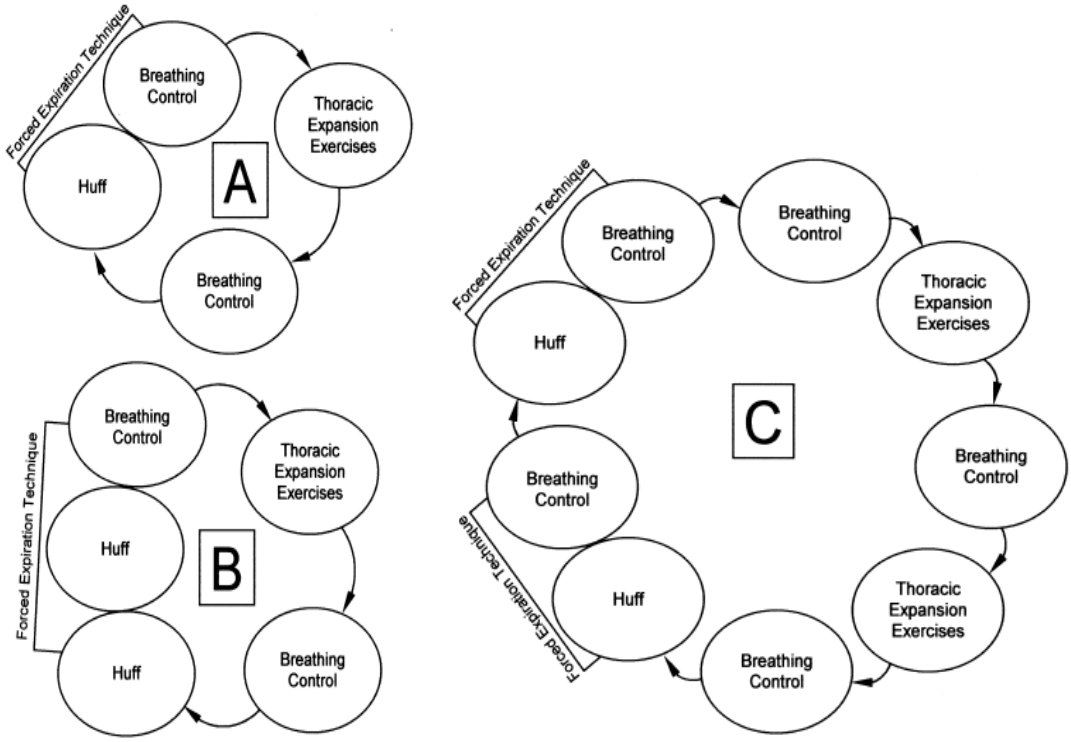
This is an active, full inspiration maneuver, followed by relaxed exhalation. It may include a 3 second inspiratory hold (hold the breath). This is done for 3-4 breaths.

FORCED EXPIRATORY TECHNIQUE

This includes 2-3 forced exhalations, followed by breathing control. The patient squeezes out air while keeping the mouth and the glottis (upper airway at the level of the Adam’s apple) open. Sometimes this is described as “pushing a tennis ball out of the mouth.” This is done at various lung volumes, so the secretions can be moved up the airways in order to be coughed out. Only 2-3 forced expiratory techniques, including the huff cough, should be performed at one time to avoid bronchospasm.



Graphic illustration showing breathing volumes during the Active Cycle Breathing Technique. Try it! KEY: IRV= inspiratory reserve volume. V_T = tidal volume. ERV = expiratory reserve volume. RV = residual volume. BC = breathing control. TEE = thoracic expansion exercise. FRC = functional residual capacity. FET = forced expiratory technique. FRC = functional residual capacity (from Lapin, C.D. Respir Care 2002; 47: 778-85).



Graphic illustration of an example of the chain of events in several rounds of ACBT. The exact number of efforts in the sequence can be individualized to the patient for best results.

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Percussion and Postural Drainage

Percussion and postural drainage (P & PD) has long been the primary method of Airway Clearance Therapy (ACT). The patient is placed in drainage positions using gravity to drain specific areas of the lungs. Percussion and vibration is then delivered to the chest wall by either cupping of the hands or a percussive device. Therapy should last up to thirty minutes with the patient changing positions throughout the session. Possible detrimental effects of P & PD in the Trendelenburg (head tilted down) position includes a drop in oxygen level, bronchospasm, acid reflux, change in heart rhythm and increased intracranial pressure (increased pressure inside the head). It also may not be recommended in patients having chest pain or unstable bones in the chest wall or spine. A properly performed treatment should last 30-45 minutes.

Advantages:

- Does not require special equipment
- Other ACT breathing techniques may be coupled with this at the same time for a more efficient, interactive therapy session
- Can be done on patients of all ages
- "Problem" areas of the lung can the target of extra focus

Disadvantage: Cannot be done independently

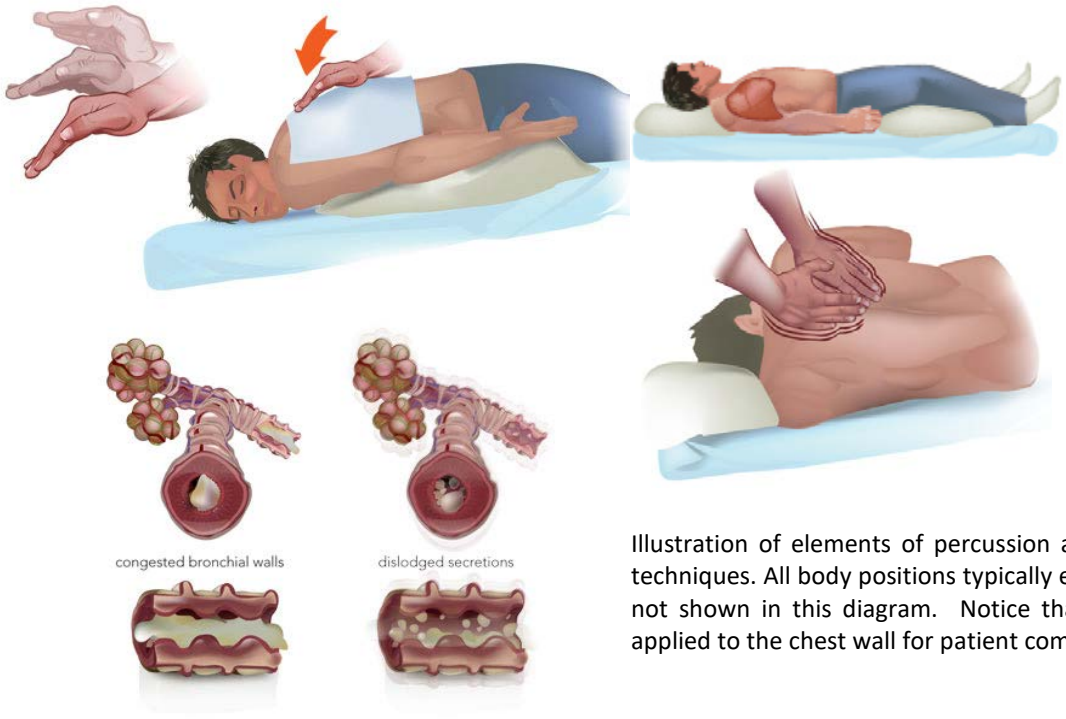


Illustration of elements of percussion and vibration techniques. All body positions typically employed are not shown in this diagram. Notice that a towel is applied to the chest wall for patient comfort.

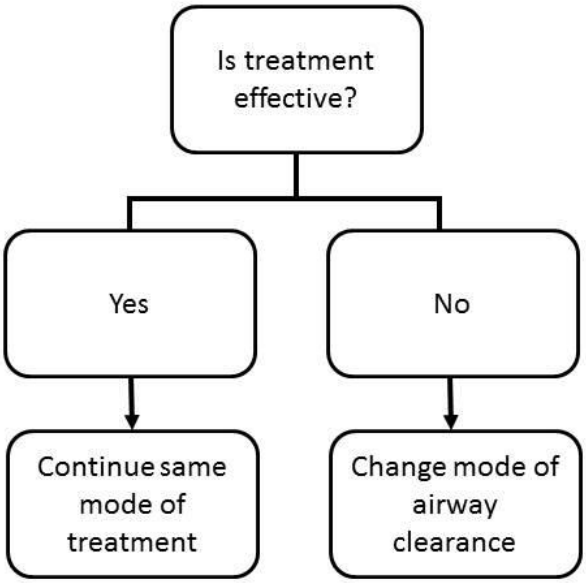
Percussion involves rhythmically striking chest wall over congested lung fields to free up airway secretions. The can be done with cupped hands (as shown in the illustrations) or commercial products like "palm cups", which can help with hand fatigue. During percussion, the fingers and thumb are held together and flexed slightly to form a cup. When the cupped hands contact the chest wall, air is trapped, propelling vibrations through the soft tissues to the airways. When performing percussion, the area being treated should be covered with a towel or the patient's gown to reduce discomfort. The patient is instructed to breathe slowly and deeply while the chest wall is rhythmically percussed.

Vibration is used after percussion or alternately with percussion to increase the turbulence of exhaled air and loosen secretions. Hands are placed over the treatment area either side by side or with one hand on top of the other and with fingers extended and together. While the patient exhales slowly through pursed lips or the nose, the hands and arm muscles and tensed and the heel of hand in contact is moved in a shaking manner to create vibrations through the patient's chest wall. When the patient inhales, stop moving your hands. Perform vibration over the affected area during five exhalations. After each vibration, the patient should cough (see section on huff cough).

Postural drainage is performed to remove secretions by gravity from different areas of the lungs. To drain the affected areas, the patient is placed in a variety of positions to facilitate drainage by gravity. Not all positions are required for every patient and our policy at Maine Medical Center is to avoid "tipping" (Trendelenburg) to avoid acid reflux and aspiration. If the patient is receiving continuous tube feedings, stop the feeding and check gastric residual at least 30 minutes before performing postural drainage or percussion. The patient usually remains in each position for 10 to 15 minutes. However, this time may be shorter initially and then gradually increased as the patient is better able to tolerate it. When performing postural drainage, first position the patient, then percuss and vibrate, then remove the secretions either by having the patient huff cough.

Sources: "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.
Images/text: https://skillsmodules.atitesting.com/SkillsModulesContent/content2/airway-management/ap4.html

Assess Effectiveness of Airway Clearance



Signs of effective treatment:

- Raising secretions (during and up to 2 hours after treatment
- Lung sounds improving
- Increased lung function on spirometry
- Improved chest x-ray
- Decreased white blood cell count
- Reduced chest congestion
- Decreased fever
- Increased energy
- Improved sense of well being

Modes of Airway Clearance:

- Airway Clearance Techniques
- Percussion
- Postural Drainage
- Vibration
- Shaking
- Vest
- Active Cycle Breathing Techniques
- Aerobika
- Autogenic Drainage
- Exercise

Chronic Pulmonary Therapies

In 2013 a multidisciplinary committee developed a consensus document to guide decision making around use of maintenance medications for CF lung disease.

DEFINITIONS OF RECOMMENDATIONS

Level A- The committee strongly recommends that clinicians routinely provide this therapy. There is high certainty that the net benefit is substantial.
Level B- The committee recommends that clinicians routinely provide this therapy. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.
Level C- The committee recommends that clinicians consider providing this therapy to selected individuals depending on individual circumstances. However, for most individuals without signs or symptoms, there is likely to be only a small benefit from this treatment.
Level D- The committee recommends against this therapy. There is moderate or high certainty that the treatment has no net benefit or that the harms outweigh the benefits. Clinicians should discourage the use of this treatment.
Level I- The committee concludes that the current evidence is insufficient to assess the balance of benefits and harms of the treatment. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

U.S. Preventive Services Task Force Evidence Grading				
Certainty of Benefit	Magnitude of Net Benefit (Benefit Minus Harm)			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I (insufficient evidence)			

Definition of Airway Disease Severity:

- Normal lung function — $FEV_1 \geq 90\%$ predicted
- Mild pulmonary impairment — FEV_1 70-89% predicted
- Moderate pulmonary impairment — FEV_1 40-69% predicted
- Severe pulmonary impairment — FEV_1 <40% predicted

RECOMMENDATIONS

Aerosolized Antibiotics: The most common respiratory pathogen in CF patients is *Pseudomonas aeruginosa* (PA). Chronic infection with this organism is associated with accelerated decline in lung function. Therefore, many centers are implementing protocols to eradicate (get rid of) this organism as soon as it is detected in sputum cultures. Once infection is established *chronic suppressive therapy* (using medications to control the side effects of infection) is recommended.

Macrolides: The mechanism of action of macrolide antibiotics is not known. *In vitro* studies suggest that there may be a decrease in production of bacterial virulence factors (chemicals released by bacteria that promote more tissue damage) and a change in host inflammatory response (how the body reacts to injury), or both, particularly in patients with *Pseudomonas aeruginosa* infections.

Antistaphylococcal Antibiotics: Staphylococcal bacteria are commonly identified in the sputum of young children with CF. Of the randomized controlled trials directed toward therapy with antistaphylococcal antibiotics, there was a reduction in *Staphylococcus* spp. in sputum cultures but no improvement in health status. There was also evidence that this therapy increased the occurrence of PA infection

Recombinant Human DNase: Airway obstruction by thickened secretions and cellular debris is the hallmark of CF lung disease. Recombinant human DNase (dornase alpha, Pulmozyme®) was developed to degrade free DNA that accumulates in mucus. This improves the viscoelastic properties of airway secretions (softens and makes it easier to break up), promoting airway clearance.

Hypertonic Saline: Malfunction of the CFTR protein on cell surfaces in CF leads to an imbalance in salt and water movement across cells. Inhalation of hypertonic saline (salty water) has been proposed as a therapy to increase hydration of the fluid layer that lines the airways of the lungs, thereby assisting with mucus clearance.

Anti-inflammatory Agents: Studies have shown that the inflammatory response (how the body reacts to injury) is excessive in CF. It is thought that this excessive and ongoing inflammation is a major cause of tissue damage in the airways over time. This leads to remodeling of the airway (bronchiectasis) and loss of lung function through airway obstruction (like asthma and COPD). Cysteinyl leukotrienes are produced by a variety of cells (eosinophils, mast cells, and macrophages) are found in increased numbers in the airway secretions of CF patients.

Bronchodilators: These medications relax smooth muscle in the walls of airways, causing them to dilate and potentially allowing improved delivery of other medications to the lungs. They are a mainstay of treatment for patients with asthmatic lung disease and COPD. In addition some of these medications increase the beat frequency of cilia (tiny hair-like projections from airway lining cells), which can improve clearance of airway secretions.

N-acetyl Cysteine: This molecule acts chemically as a reducing agent, donating hydrogens and breaking disulfide bonds. In practical terms, it works like meat tenderizer, softening up thick secretions. In theory this should decrease mucus viscosity and improve airway clearance.

Small Molecule Agents: Two major classes of "small molecule" agents are radically changing the face of therapy for CF. The first category of medications includes "*potentiators*," which work by "dialing up" the activity of surface-expressed CFTR. Ivacaftor is the first commercially available potentiator that was initially studied in patients with the G551D mutation in CFTR. The medication is now FDA-approved for a number of other mutations. The second class of medications are designated "*correctors*". These medications increase the amount of CFTR protein (the dysfunctional protein in CF) expressed on the surface of cells that are in charge of salt and water transport. Lumacaftor is the first commercially available corrector that was first studied in combination with ivacaftor to treat patients having two copies of the F508del mutation (the most common mutation to cause CF). Additional small molecule agents are being developed that promise to be more effective and have fewer side effects than the first generation potentiators and correctors.

Grading of Benefit for Commonly Used Medications: The following table uses the U.S. Preventive Services Task Force evidence grading approach to classify the net benefit of various medical therapies for CF.

Agent	Indication	Assessing Net Benefit	Grade
Inhaled Tobramycin	• ≥ 6 years of age • Moderate-severe lung disease • Chronic PA infection	• Certainty: High • Estimate: Substantial	**A**
	• ≥ 6 years of age • Asymptomatic or mild lung disease • Chronic PA infection	• Certainty: Moderate • Estimate: Moderate	B
Inhaled Aztreonam	• ≥ 6 years of age • Moderate-severe lung disease • Chronic PA infection	• Certainty: High • Estimate: Substantial	A
	• ≥ 6 years of age • Mild lung disease • Chronic PA infection	• Certainty: Moderate • Estimate: Moderate	B
Other inhaled antibiotics (e.g., amikacin, carbenicillin, ceftazidime, colistin, gentamicin)	• ≥ 6 years of age • Chronic PA infection	• Certainty: Low • Estimate: None	I
Oral anti-pseudomonal antibiotics	• ≥ 6 years of age • Chronic PA infection	• Certainty: Low • Estimate: None	I
Recombinant Human DNase	• ≥ 6 years of age • Moderate-severe lung disease	• Certainty: High • Estimate: Substantial	A
	• ≥ 6 years of age • Asymptomatic or mild lung disease • Chronic PA infection	• Certainty: Moderate • Estimate: Moderate	B
Hypertonic Saline	• ≥ 6 years of age	• Certainty: Moderate • Estimate: Moderate	B

Inhaled Corticosteroids	• ≥ 6 years of age • Without asthma or Allergic Bronchopulmonary Aspergillosis	• Certainty: High • Estimate: zero	D
Oral steroids	• ≥ 6 years of age • Without asthma or Allergic Bronchopulmonary Aspergillosis	• Certainty: High • Estimate: zero	D
Ibuprofen	• ≥ 18 years of age	• Certainty: Low • Estimate: None	I
Leukotriene Inhibitors	• ≥ 6 years of age	• Certainty: Low • Estimate: None	I
Cromolyn	• ≥ 6 years of age	• Certainty: Low • Estimate: None	I
Azithromycin	• ≥ 6 years of age • Chronic PA infection	• Certainty: High • Estimate: Moderate	B
	• ≥ 6 years of age • Without PA infection	• Certainty: Moderate • Estimate: Small	C
Oral Antistaphylococcal antibiotics	• Any age	• Certainty: Moderate • Estimate: Negative	D
Oral Antistaphylococcal antibiotics	• Any age • Chronic SA infection	• Certainty: Low • Estimate: None	I
Inhaled b_2-agonists	• ≥ 6 years of age • Without asthma	• Certainty: Low • Estimate: None	I
Inhaled anticholinergics	• ≥ 6 years of age • Without asthma	• Certainty: Low • Estimate: None	I
Inhaled or oral N-acetyl-cysteine	• ≥ 6 years of age	• Certainty: Low • Estimate: None	I

Ivacaftor	● ≥ 6 years of age ● Appropriate CFTR mutation	● Certainty: High ● Estimate: Substantial	A
Other CFTR modulator therapies	● This area is evolving	This area is evolving	

Source: Cystic Fibrosis Pulmonary Guidelines "Chronic Medications for Maintenance of Lung Health". Mogayzel et al. Am J Respir Crit Care Med 2013 Apr;187(7):680-9. http://www.ncbi.nlm.nih.gov/pubmed/23540878

Hemoptysis

The occurrence of hemoptysis, or coughing up blood, often raises questions from patients, family and staff members. Qualitatively, hemoptysis can be categorized as little more than an annoyance up to a life threatening event. The CF Foundation Pulmonary Therapies Committee has graded hemoptysis by consensus as follows:

- Scant < 5 mL
- Mild to moderate 5-240 mL
- Massive >240 mL

Some authorities also define >100 mL blood expectorated during a single episode as massive hemoptysis. Coughing blood usually is associated with a flare of lower airway infection and inflammation. Therefore therapy usually includes treatment for pulmonary exacerbation along with treatments that may be more specifically targeted to stop bleeding. Lung tissue is fed by two circulatory systems, the bronchial arteries and the pulmonary arteries. The pulmonary arteries receive blood from the right side of the heart and typically blood flows through these arteries at a relatively low pressure. The bronchial arteries, on the other hand, derive from the aorta, which funnels blood from the left side of the heart at higher blood pressure. In the case of moderate to massive hemoptysis, we are most concerned about bronchial arterial bleeding. The bronchial arteries tend to become ectatic (twisted and gnarled) due to neovascular changes (stimulation of new blood vessel growth) in areas of inflamed lung. These new, tangled blood vessels can be fragile and more likely to bleed. Remember, patients with massive hemoptysis more commonly die from asphyxiation (choking on blood clots) than exsanguination (blood loss), so careful monitoring and management of the airway is most important.

DIAGNOSTIC WORKUP

A number of things should be routinely checked in patients with moderate to massive hemoptysis. It is worth mentioning that all expectorated blood does not necessarily derive from the lungs—be sure to take a careful history and perform a directed physical exam to rule out bleeding from an extra-pulmonary source (e.g., gastrointestinal or nasal/upper airway). Then proceed with the following:

- Chest x-ray
- CBC (including platelet count)
- Consider an arterial blood gas if the patient appears unstable
- INR (vitamin K deficiency is quite common)

- Medication list—particularly pay attention to anticoagulants and non-steroidal anti-inflammatory medications
- Request consultation by the Pulmonary Service

In certain circumstances, it may be helpful to get more detailed imaging of the chest with a CT scan. Unless pulmonary embolism is in the differential diagnosis, it is generally best to get a NON-CONTRAST chest CT. Bronchoscopy is not usually needed for evaluation of hemoptysis in CF patients because lung cancer is typically not in the differential diagnosis. The Pulmonary Consult Service should be involved in review of the CT scan and decisions about further workup and treatment of moderate to massive hemoptysis.

TREATMENT

The following general guidelines are offered for treatment of moderate to massive hemoptysis. Again, consultation with the Pulmonary Service is recommended in order to optimize individual therapy.

- Stop all anticoagulant medications and non-steroidal anti-inflammatory medications
- Reverse vitamin K deficiency
- Consider bronchial artery embolization as both a diagnostic and therapeutic maneuver. Bronchial arteries are accessed by running an arterial catheter from the femoral artery up through the aorta to the take-off of the bronchial arteries. Care must be taken to avoid the spinal arteries. Collaterals from intercostal arteries can also be sources of bleeding. Contrast is used to navigate to the proper position and all ectatic vessels are treated if possible. This is why it is helpful to avoid using contrast on the chest CT if possible to minimize the chance of renal injury. Post procedure, patients should be checked carefully for any neurologic changes from baseline and assessed for chest pain.

Bronchial artery embolization showing “blush” due to ectatic blood vessels (left panel) and “stasis” or no blush after embolization (right panel).
Source: https://www.slideshare.net/sabharisundaravel/bronchial-artery-embolisation-in-haemoptysis

BILEVEL POSITIVE AIRWAY PRESSURE (BiPAP)

Patients with advanced lung disease are often supported with BiPAP therapy through a nasal or face mask at night. In the setting of hemoptysis, there is often question about whether BiPAP should be used.

Recommendations:

- BiPAP should not be withheld from patients with *scant* hemoptysis
- BiPAP should be withheld from patients with *massive* hemoptysis
- In most cases of *mild to moderate* hemoptysis, BiPAP can be continued as an important part of therapy to treat underlying lung infection

AIRWAY CLEARANCE AND AEROSOL THERAPIES

Recommendations:

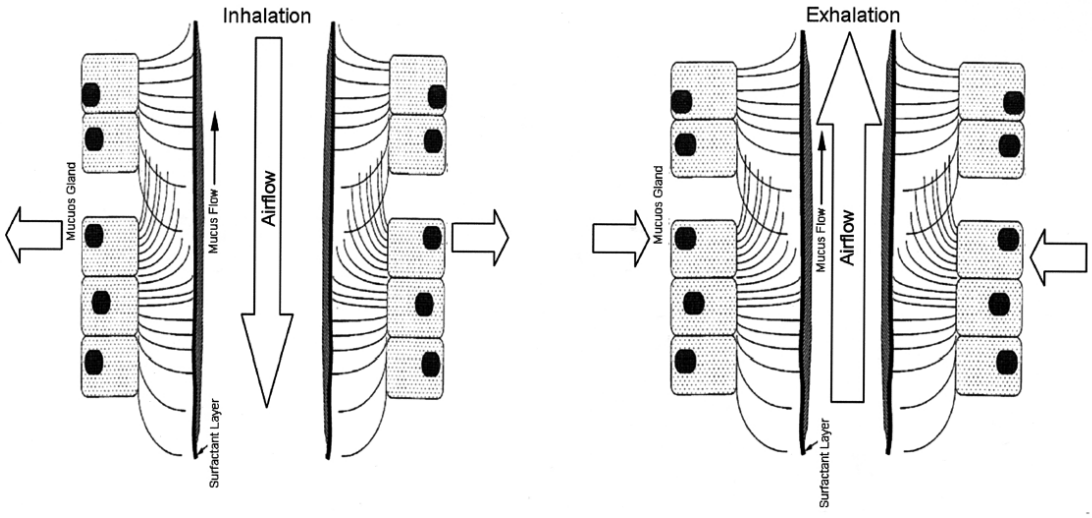
- Airway clearance therapies should not be withheld from patients with *scant* hemoptysis
- Airway clearance therapies should be withheld from patients with *massive* hemoptysis
- In most cases of *mild to moderate* hemoptysis, airway clearance can be continued as an important part of therapy to treat underlying lung infection
- Aerosol therapies should not be withheld from patients with *scant* hemoptysis
- Hypertonic saline treatment should be stopped in patients with *massive* hemoptysis
- The consensus recommendation is that hypertonic saline may induce cough and possibly exacerbate massive hemoptysis, and the benefits of continuing prescribed aerosol therapies outweighs the risks and should only be withheld if they seem to exaggerate or provoke bleeding

Source: Adapted from Richards, K, Seidelman, J, Lester, M. Cystic Fibrosis Respiratory 101: Getting Started. 2017.

Huff Cough Technique

HUFF COUGH

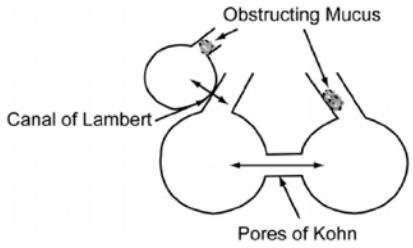
A central component of any airway clearance technique for CF patients (be it related to chest physical therapy, active cycle breathing technique, oscillatory PEP device or high frequency chest wall oscillation) is an effective cough. The "huff cough" is a controlled way of maneuver that tries to take advantage of the shearing force of vigorous, active exhalation while trying to prevent airway collapse. The size of the breath and the length and force of exhalation is changed to maximize airflow. Keeping the glottis open (the part of the airway at the level of the Adam's apple) is key and can be learned with practice.



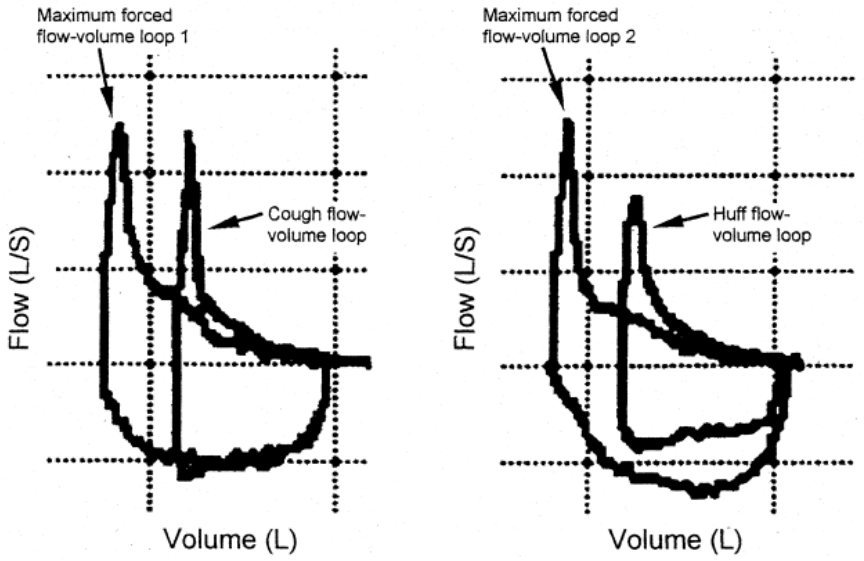
The illustration shows that with normal mucociliary function, greater energy is applied to the mucus layer during expiration because of airway narrowing during this phase of breathing. This creates a shearing force on the mucus to help remove it from the airway wall. (from Fink, JB. Respir Care 2007; 52: 1210-21).

TECHNIQUE FOR HUFF COUGH

- Sit up straight for optimal lung expansion
- Inhale slowly--the volume of inhaled air can be modified depending on the targeted airway size
- Hold breath for 2-3 seconds for optimal air distribution throughout the airways and to allow air to get behind the mucus using collateral ventilation pathways



Cartoon showing how collateral ventilation can be used to mobilize mucus (reference shown below)



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Flow-volume curves comparing voluntary cough (left panel) and huff cough (right). Notice how the huff maneuver is performed at lower airflows than with usual cough and maximum flow during lung function testing. While there is a bit lower airflow at the peak, this may prevent large airway collapse (from Lapin, C.D. Respir Care 2002; 47: 778-85).

Advantages

- Should be done in conjunction with other airway clearance techniques such as percussion and postural drainage, Vest use, etc.
- Does not require expensive equipment
- Patient can adjust the technique to their specific, daily mucus production
- Greater independence

Disadvantages

- Patient must be able to concentrate appropriately and consistently on proper technique

Sources:

"Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

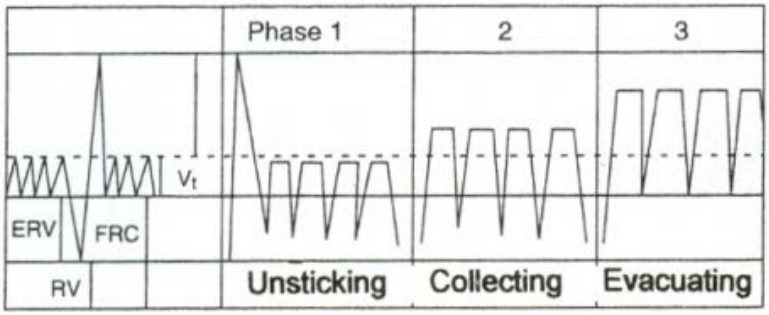
Collateral ventilation cartoon:
https://www.researchgate.net/profile/Brian_Walsh8/publication/51671780/figure/fig2/AS:306000247705600@1449967552123/Fig-2-Alveolar-collateral-channels-in-older-children-and-adults-facilitate-gas-exchange.png

Autogenic Drainage Technique

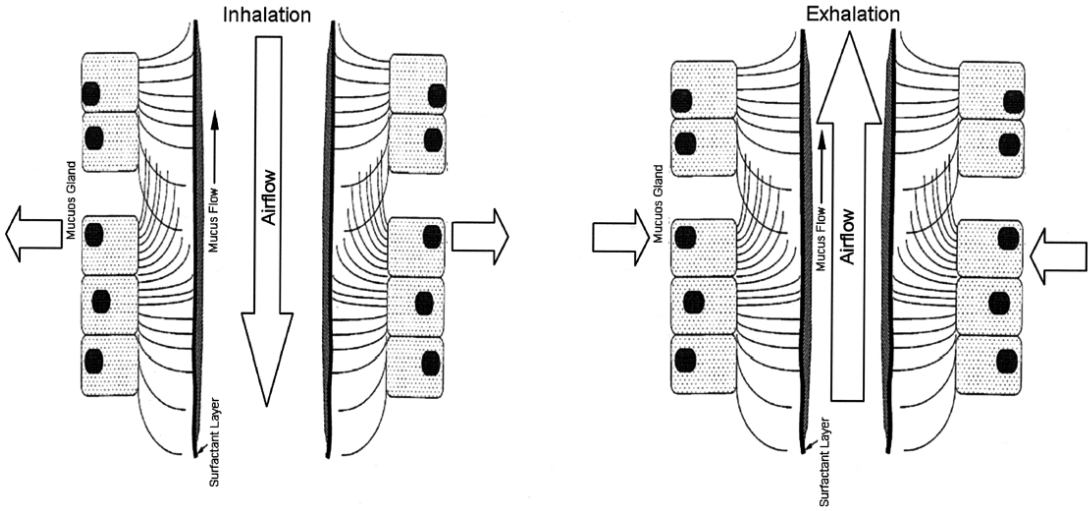
AUTOGENIC DRAINAGE

This is a breathing exercise that incorporates controlled breathing at different lung volumes to promote movement of secretions from small airways to larger, more central airways. While this technique can be highly effective and works well for patients who are active and seek independence, it can be tricky to learn--a bit like learning to play a musical instrument or sing well. There are three stages to the method:

1. Unsticking, which is done with tidal breathing at low lung volumes
2. Collecting, which is done with tidal breathing at mid-lung volumes
3. Evacuation, which is done at tidal breathing at large lung volumes



Graphic depiction of breathing at different lung volumes during different phases of autogenic drainage (from Hardy, KA. Respir Care 1994; 39:440-452).



The illustration shows that with normal mucociliary function, greater energy is applied to the mucus layer during expiration because of airway narrowing during this phase of breathing. This creates a shearing force on the mucus to help remove it from the airway wall. (from Fink, JB. Respir Care 2007; 52: 1210-21).

TECHNIQUE

The following is a narrative description for patients on how to perform autogenic drainage:

- Take a slow, normal, tidal breath in through the nose; hold for 3-4 seconds; then exhale through the mouth with an open glottis, completely. Repeat for 3-4 breaths or until you hear the mucus become “loose”
- Then take a slow, larger breath through the nose; hold breath for 3-4 seconds; then exhale with an open glottis, until almost completely out. Repeat for 3-4 breaths
- Take a slow, even larger breath to fully inflate the lungs; hold for 3-4 seconds; then exhale with an open glottis to a normal lung volume (where you rest after a normal breath). Repeat for 3-4 breaths
- Try to suppress the cough until the end of the third stage
- Exhale as fast as possible without causing airway collapse (huff cough) or wheezing
- Always listen for “loose” mucus to know when to move on to the next phase

Advantages:

- Can be done anywhere independently
- Does not require expensive equipment

Disadvantages:

- Patient must be able to concentrate and follow directions to master this technique
- Not recommended for patients with advanced lung disease

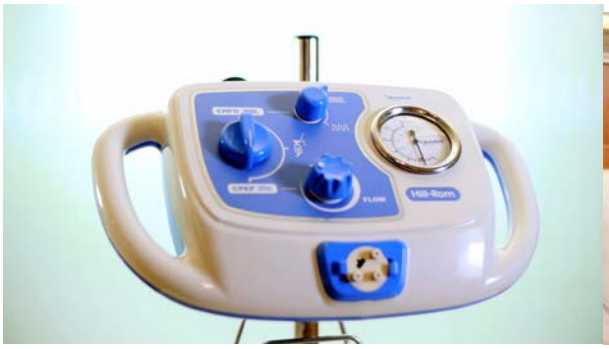
Adapted from “Cystic Fibrosis Respiratory 101: Getting Started” syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

MetaNeb®

THE METANEB® SYSTEM

This device allows for simultaneous aerosol delivery through a Salter nebulizer and supplemental oxygen, when needed, while it provides airway clearance. While there is appeal in its design, particularly for in hospital use, it is still relatively new and there are limited studies to support its broader application. It is indicated for mucus mobilization and airway clearance as well as lung expansion to treat or prevent atelectasis. The device has 3 modes:

- Aerosol only
- Continuous Positive Expiratory Pressure (CPEP)--This mode allows for delivery of a chosen set positive airway pressure (PAP) that is consistent throughout inspiration and expiration. PAP is set by using a constant flow with a venturi and expiratory resistor
- Continuous High Frequency Oscillation (CHFO)--This mode uses oscillations throughout inspiration and expiration (170-230 breaths per minute), combined with PEP to aid with airway clearance.



MetaNeb® System for simultaneous delivery of aerosolized medication and oxygen while providing airway clearance.
https://www.hill-rom.com/usa/Products/Category/Respiratory-Care/MetaNeb-System/

TECHNIQUE

A thorough treatment involves use of CPEP and CHFO modes, as follows:

- Perform function check

- Have patient sit in an upright position with elbows on the table, if possible
- Fill nebulizer cup with medication. MetaNeb® aerosolizes 0.5 ml/min of medication. Therefore, a 10 minute therapy session will need 5-6 ml of solution
- Select CPEP mode and rotate resistor ring to the middle position
- Prior to providing to the patient, occlude the mouthpiece and adjust the CPEP to the goal pressure (starting at 5-10 cm H_2O. Pressure may be titrated upwards to 20 cm cm H_2O, as the patient tolerates)
- Ask the patient to exhale slowly over 3-4 seconds

Advantages:

- Can deliver medication while providing airway clearance
- May be performed semi-independently

Disadvantages:

- Expensive and not very portable (needs a power source)
- At least in theory there may be concern about mucus impaction and/or barotrauma from positive airway pressure

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Nebulizer Selection

JET NEBULIZERS

Jet nebulization is a process whereby a high-velocity gas jet fragments a film of liquid into droplets of varying sizes. Forcing air through an extremely small orifice generates the high-velocity jet. Droplets that are too large to be inhaled hit baffles inside the nebulizer and return to the liquid to be re-nebulized. The standard unvented nebulizer (T-piece) has only one inlet, which is the driving flow for the nebulizer and has one outlet, which is a T-piece and mouthpiece.

T-piece nebulizer

Advantages:

- Output is independent of patient effort or respiratory status
- Inexpensive

Disadvantages:

- The aerosol is diluted as extra air is inhaled through the back of the T-piece
- Degradation of particle size distribution with repeated use (less consistent size of droplets)
- Plastic cannot withstand the proper cleaning and disinfection guidelines of the CF Foundation
- Decreased portability, as they require a compressor (that forces gas through the nebulizer) that requires an AC outlet or batteries

SIDESTREAM®NEBULIZER

This nebulizer uses another method to shear the liquid solution into an aerosol. Instead of directing the gas stream on the liquid at a 90 degree angle, the gas stream is directed over the surface of the liquid. Air is drawn into the nebulizer all during nebulization.

Sidestream nebulizer

Advantages:

- Output is independent on the patient's respiratory status
- Approved for use with Pulmozyme®
- Can tolerate cleaning and disinfection by CF Foundation guidelines
- Longer warranty than disposable nebulizers

Disadvantages:

- More waste of medication during exhalation (ok for some medications like bronchodilators, hypertonic saline, and dornase alpha, but not good for dose dependent medications like antibiotics)
- Decreased portability, as they require a compressor (that forces gas through the nebulizer) that requires an AC outlet or batteries

BREATH-ENHANCED NEBULIZERS

These nebulizers minimize drug loss during exhalation by entraining the inspiratory flow of the patient through the nebulizer. This action causes particles that would normally "rain out" (condense along the walls of the device, like fog condenses on a cold windshield) when using a standard nebulizer to be swept away because of enhanced flow through the nebulizer during inspiration. During exhalation, increased rain-out occurs and the drug returns to the reservoir for renebulization. The Pari LC Plus® and Pari LC Star® are examples of this type of nebulizer.

Pari LC nebulizer

Advantages:

- Delivers 2-4 times more medication to the lung than a T-piece or Sidestream® nebulizer
- Less waste of medication
- The Pari LC Plus® is the nebulizer approved for use with TOBI® and Pulmozyme®
- Able to clean and disinfect following guidelines of the CF Foundation
- Longer warranty than disposable nebulizers

Disadvantages

- Decreased portability, as they require a compressor (that forces gas through the nebulizer) that requires an AC outlet or batteries

COMPRESSORS

A jet nebulizer is powered by an electric compressor to make an aerosol. When considering administration of medications for patients at home, a decision needs to be made regarding the combination of both the nebulizer and the compressor. Particle size and output may vary when using different combinations of nebulizer/compressor systems. Most common compressors perform the same regarding nebulizer output. While some very powerful compressors can generate high pressures and airflow, resulting in smaller droplets and shorter treatment times, more drug is wasted during exhalation. Battery operated compressors make traveling

more convenient but are not as powerful. The lower pressures make larger droplets and may decrease deposition of medication into the lungs and also result in longer treatment times.

WHICH NEBULIZER FOR WHICH DRUG?

Nebulizer	Drugs
T-piece	As recommended by your physician
Sidestream®(use with 50 PSI compressor, such as MobilAire®)	Pulmozyme®(dornase alpha) Albuterol (salbutamol)
Pari LC Plus®(use with 25 PSI compressor, such as PulmoAide®)	TOBI® Colymycin (colistimethate sodium, USP) Albuterol Pulmozyme® Pulmicort Respules®(budesonide suspension)
Pari LC Star®(use with 25 PSI compressor, such as PulmoAide®)	Colymycin Albuterol Pulmozyme® Pulmicort Respules®(budesonide suspension)

ORDER OF AEROSOLIZED THERAPIES

Many patients benefit from using multiple therapies, and therefore the question often arises about the correct order for these treatments. Few studies have addressed the appropriate order of aerosolized therapies. Most studies that were evaluated by the multidisciplinary committee assembled by the CF Foundation included patients receiving a wide variety of medications. There is *in vitro* (in the laboratory) data showing that dornase alfa is inactivated by high salt concentrations, but it is not clear if this effect occurs *in vivo* (in living animals). Others have argued that inhaled antibiotics are expensive agents that work most effectively when they reach deep into lung tissue, so the airways should first be opened and maximally cleared of mucus. This is the currently recommended order:

Bronchodilators
Hypertonic Saline
Dornase Alfa (Pulmozyme®)
Aerosolized Antibiotics

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Positive Expiratory Pressure Devices

POSITIVE EXPIRATORY PRESSURE (PEP) DEVICES

PEP devices come in lots of shapes and sizes. The basic principle of these instruments is to maintain positive pressure in the airways so as to prevent airway collapse during exhalation. Each device, at its core, contains a resistor that impedes the flow of air out of the lungs during exhalation. By doing that, airway pressure is kept elevated (typically in the range of 10-25 cm H2O), pushing air through regions of collateral ventilation (see section on Active Cycle Breathing) and helping to "pop" mucus plugs out of obstructed airways. Airway oscillating devices (AODs) are handheld devices that provide PEP and vibration within the airways to help with mucus clearance. These accessories tend to be more popular than the static devices that were more frequently used in the past.

EXAMPLES

Examples of some popular AODs. Aerobika® (left), Acapella® (middle), and Flutter® (right)

TECHNIQUE

The following is a narrative description for patients on how to use an AOD:

- Sit in an upright position
- Breath in with the device in your mouth; hold your breath for 3 seconds, then exhale for at least 4 seconds while keeping your cheeks tight
- Adjust resistance on your device (for Aerobika® and Acapella®) as needed to comfortably exhale as instructed
- Repeat for ten breaths; then huff cough
- Repeat this cycle for at least 20 minutes

Advantages:

- Can be done almost anywhere independently
- Does not require expensive equipment
- Some devices, like the Aerobika®, can be hooked up to a nebulizer and compressor, so that some medical treatments can be completed while doing airway clearance

Disadvantages:

- Patient must be able to generate sufficient airflow for the equipment to operate as designed
- Not recommended for patients with advanced lung disease

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Pneumothorax

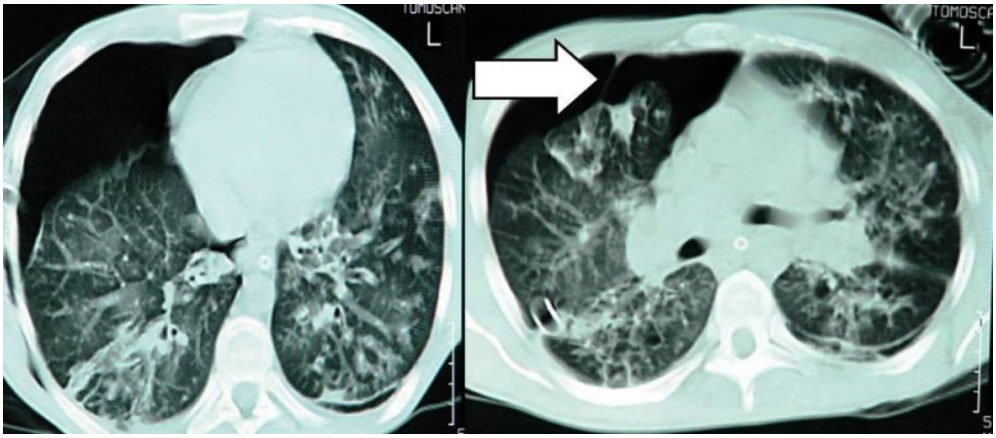
According to the 2016 CF Patient Registry, the annual incidence of pneumothorax (lung collapse due to a hole in the surface or pleura of the lung) in CF adults is 0.4% and the lifetime frequency of this condition is 3.4%. It is more common in older patients with severe lung disease, particularly those who have FEV1 < 30% predicted, and those infected with *Pseudomonas aeruginosa, Burkholderia cepacia* complex, or *Aspergillus* spp. Pneumothorax may also be more likely in those who use positive airway pressure devices (for example, BiPAP). Patients most often complain about shortness of breath, chest tightness and chest pain.

Size definition:

- Small: ≤3 cm from the surface of the lungs to the inside of the ribs markings on a chest x-ray
- Large: >3 cm

DIAGNOSTIC WORKUP

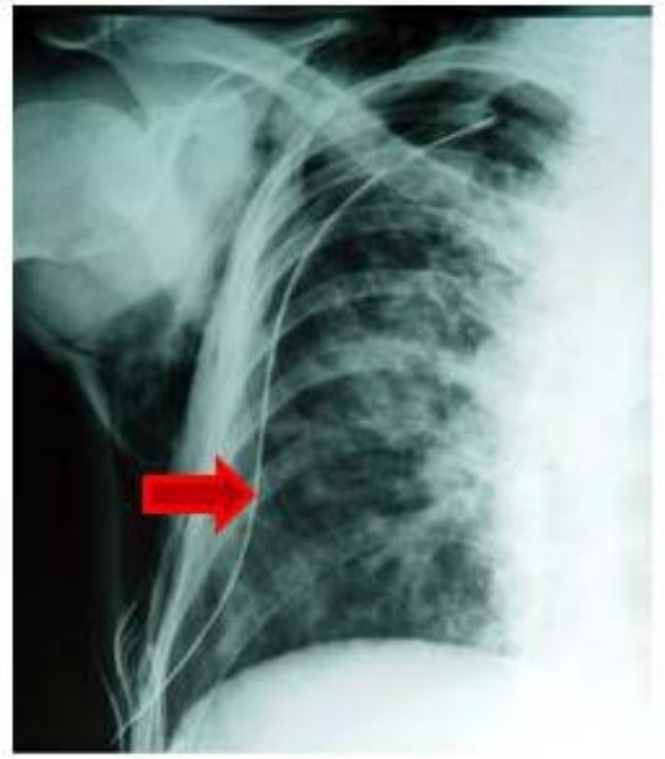
The first order of business is to assess patient stability. Vital signs, including measurement of oxyhemoglobin saturation, should be taken. If there is bedside evidence of lung collapse leading to a so called "tension pneumothorax" (increase in pulsus paradoxus to >10 mm Hg, hypotension, absent breath sounds on one side of the chest, etc.), then the patient should be treated emergently with chest tube placement without delay. Bedside ultrasound may be useful to confirm tension physiology and guide placement of the tube. Chest tube placement is beyond the scope of this manual but should be placed by an emergency room physician, thoracic surgeon or pulmonary specialist (see additional information in the section on treatment). Chest x-ray is usually the first diagnostic test in patients who are clinically stable. In some cases, it may be helpful to obtain a non-contrast chest CT to evaluate for more complex disease, where the pneumothorax may be loculated.



Axial chest CT images showing a loculated pneumothorax (lung prevented from fully collapsing by adhesive scar tissue, shown by the arrow). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203988/figure/f1/

TREATMENT

Patients with small pneumothoraces can often be treated with supplemental oxygen and observation only. Supplemental oxygen is used to help wash nitrogen out of the "bubble of air" in the chest and speed the resolution of the pneumothorax. However, if the patient remains symptomatic or has progression to a larger pneumothorax, then a chest tube should be placed. Sometimes the pneumothorax will resolve and be adequately treated with chest tube placement alone. In other instances, additional treatment, called pleurodesis (whereby the surface of the lung is made to "stick" to the inside of the chest wall so that pneumothorax does not recur). Different types and sizes of tubes should be considered, depending on the size and location of the pneumothorax and the patient's clinical status. Pulmonary consultation should be obtained to assist with decision-making around chest tube placement and pleurodesis.



Chest x-ray showing a right sided chest tube (red arrow) placed for pneumothorax.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203988/figure/f2/

BILEVEL POSITIVE AIRWAY PRESSURE (BiPAP)

Patients with advanced lung disease are often supported with BiPAP therapy through a nasal or face mask at night. In the setting of pneumothorax, there is often question about whether BiPAP should be used.

Recommendation: BiPAP should be withheld from patients with pneumothorax as long as the pneumothorax is present

AIRWAY CLEARANCE AND AEROSOL THERAPIES

Recommendations:

- Some airway clearance therapies, specifically positive expiratory and intrapulmonary percussive ventilation, should not be used in patients with pneumothorax. Consensus is that if a small pneumothorax is present, airway clearance therapies should continue since obstructed airways can prevent lung re-expansion and lead to clinical worsening. In the case of a large pneumothorax, airway clearance methods that utilize positive pressure in the airways should not be performed. Those include PEP, oscillating PEP, and intrapulmonary percussive ventilation (IPV).
- Withholding airway clearance therapies is not necessary if a functioning chest tube is present
- Aerosol therapies should be continued, unless a particular therapy causes greater than usual cough

GENERAL CONSENSUS RECOMMENDATIONS

- Patients with pneumothorax should not fly on a plane for 2 weeks after pneumothorax has resolved (unless pleurodesis has been performed)
- Patients with pneumothorax should not lift weights (>5 lbs) for 2 weeks after the pneumothorax has resolved (unless pleurodesis has been performed)
- Patients with pneumothorax should not perform spirometry for 2 weeks after the pneumothorax has resolved (unless pleurodesis has been performed)

Sources: Adapted from Richards, K, Seidelman, J, Lester, M. Cystic Fibrosis Respiratory 101: Getting Started. 2017.
Kioumis IP, et al. J Thorac Dis. 2014 Oct; 6(Suppl 4): S480–S487.

3 Minute Step Test

Items needed:

- Step- 30 cm or 12 inches for adults
- Metronome- 24 steps per minute or 96 beats per minute for adults
- Stop Watch
- Heart rate monitor (or you can take it manually)

Procedure:

- Demonstrate alternating steps to patient to the beat of the metronome
    - At first beat step up with one leg
    - At second beat step up with second leg
    - At third beat step down with first leg
    - At fourth beat step down with second leg
- Allow patient to practice to the beat
- Perform step test for 3 minutes – may change lead foot half way through to limit fatigue
- After 3 minutes have the patient immediately sit down
- Within 5 seconds take patients heart rate for 1 full minute
- Their heart rate is their "score"

Scoring:

- 3 Minute Step Test Category – Males
    - Excellent <71
    - Good 71-102
    - Fair 103-117
    - Poor 118-147
    - *Very Poor 148+*

- 3 Minute Step Test Category – Females
    - Excellent <97
    - Good 97-127
    - Fair 128-142
    - Poor 143-171
    - *Very Poor 172+*

Ratings for Men, Based on Age

	18-25	26-35	36-45	46-55	56-65	65+
Excellent	50-76	51-76	49-76	56-82	60-77	59-81
Good	79-84	79-85	80-88	87-93	86-94	87-92
Above Average	88-93	88-94	92-88	95-101	97-100	94-102
Average	95-100	96-102	100-105	103-111	103-109	104-110
Below Average	102-107	104-110	108-113	113-119	111-117	114-118
Poor	111-119	114-121	116-124	121-126	119-128	121-126
Very Poor	124-157	126-161	130-163	131-159	131-154	130-151

Ratings for Women, Based on Age

	18-25	26-35	36-45	46-55	56-65	65+

Excellent	52-81	58-80	51-84	63-91	60-92	70-92
Good	85-93	85-92	89-96	95-101	97-103	96-101
Above Average	96-102	95-101	100-104	104-110	106-111	104-111
Average	104-110	104-110	107-112	113-118	113-118	116-121
Below Average	113-120	113-119	115-120	120-124	119-127	123-126
Poor	122-131	122-129	124-132	126-132	129-135	128-133
Very Poor	135-169	134-171	137-169	137-171	141-174	135-155

This can show a training effect if an exercise program has been started, or a decline if health declines or exercise is stopped.

High Frequency Chest Compressors

HIGH FREQUENCY CHEST COMPRESSORS (HFCC)

These devices have been commercially available since the 1908's and are now sold by a number of companies. The traditional concept involves a wearable vest that inflates and deflates using high frequency oscillations that when transmitted to the chest wall vibrates the airways and loosens mucus. Some newer models do not use vest inflation to achieve chest vibration (Monarch and Afflovest models).

EXAMPLES

Examples of popular HFCCs. Top Row: Hill-Rom, The Vest (left), Hill-Rom, Monarch, (middle), Electromed, Smart Vest (right); Bottom Row: Resp Innovation, RespIn 11 (left), International Biophysics Corp, Afflovest (middle), Respirtech, The InCourage System (right)

TECHNIQUE

The HFCC should be properly fitted and worn with a snug fit so that the vest engages the chest wall without slipping. Vibration frequency should be varied over the course of a 30 minute airway clearance session in order generate resonant movement of different sized airways. One popular protocol, designated the Minnesota Protocol, for the traditional Hill-Rom HFCC (The Vest). Settings include the baseline inflation pressure of the vest that engages the chest wall ("pressure") and the frequency of vibration ("Hz").

Minnesota Protocol settings for The Vest:

Session 1 (15 minutes)

- Hz=6, pressure=10: for 5 minutes then pause to huff cough
- Hz=8, pressure=10: for 5 minutes then pause to huff cough
- Hz=10, pressure=10: for 5 minutes then pause to huff cough

Session 2 (15 minutes)

- Hz=16, pressure=6: for 5 minutes then pause to huff cough
- Hz=18, pressure=6: for 5 minutes then pause to huff cough
- Hz=20, pressure=6: for 5 minutes then pause to huff cough

Advantages:

- Use of HFCC for airway clearance promotes independence
- Patients can do other inhalation treatments while receiving airway clearance
- New models are portable
- Companies will typically supply new vests over the course of the patient's life
- Provides consistent therapy, independent of the patient or caregiver

Disadvantages:

- Expensive: cost ranges from $12,000-18,000
- Discomfort related to vibration over feeding tube or port sites
- Decreased portability compared to breathing techniques or airway oscillating devices

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

The Frequencer™ and Hand-held Percussor

HAND-HELD DEVICES

These devices have been marketed primarily for patients who have more advanced lung disease and trouble tolerating more vigorous airway clearance methods like vest-applied HFCC or manual chest percussion. These devices are thought to reduce mucus viscosity through resonant vibrations.

EXAMPLES

Examples of hand-held devices for airway clearance. The Frequencer™ (left) and the G5™ Vibracare® (right)

The Frequencer™ is a digitally controlled acoustical airway clearance device with two parts, a control unit and transducer. The forcing frequency can be varied from 30-70 Hz. Similarly, the G5 percussor/vibrator has a forcing frequency of 20-50 Hz.

Advantages:

- To a limited extent, each of these devices can be self administered (all lung zones cannot be reached without assistance)
- Patients can do other inhalation treatments while receiving airway clearance
- These devices are portable
- May be better tolerated by patients with chest wall pain

Disadvantages:

- Much more expensive than AODs though prices vary by vendor
- Less portable than AODs
- For the Frequencer, approximately 4 lbs. of force is needed to maintain an acoustic seal to the chest

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Vascular Access Devices

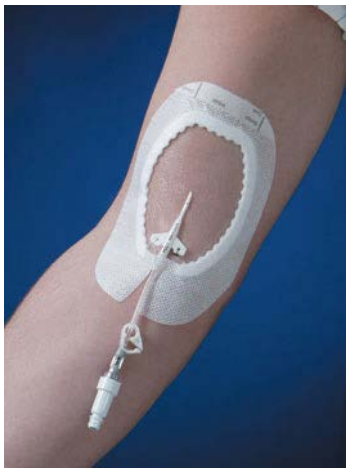
This document is written primarily for patients and families, though healthcare providers may also wish to review this material as well. Much of the content is drawn from the Adult Guide to Cystic Fibrosis that was published by the CF Foundation in 2017. Additional information is provided in the Online Resources section.

TYPES OF VASCULAR ACCESS DEVICES (VADs)

Although there are many different types and brands of VADS, the two main categories in use are peripherally inserted central venous catheters (PICCs) and totally implanted vascular access devices (TIVADs-- also commonly called "ports"). PICCs are usually selected for short courses of intravenous (IV) therapy that may go for 2-3 weeks. Ports may be used for longer term therapy, as discussed in more detail below.

PICCs

PICCs are intended for temporary use--usually for a number of weeks. They're a good choice for people who need therapy only once or twice a year (or less frequently). The PICC may be placed either in a small, dedicated procedure room or in a radiology suite, depending on your needs. A PICC is typically inserted into a vein in the crook of the elbow or the upper arm, then secured to the skin with an adhesive patch. Sometimes the catheter is placed in the side of the neck or near the collarbone. Suitable veins are typically identified using ultrasound (which does not involve any radiation). Sometimes, in more challenging cases, fluoroscopy is used (which is an x-ray video) to guide catheter placement. The insertion site is then covered with a small dressing. You may hear the term "midline" catheter. This is a type of catheter that is like a PICC but is a bit shorter.



Single lumen PICC placed in a common location in the upper extremity

The dressing is important, because PICCs must stay clean and dry at all times. You can do most activities with a PICC in place, though we recommend against swimming and activities involving the arms (like chopping wood, racquet sports, baseball, football, etc.). These types of vigorous activities may lead to irritation of the veins of the arms and shoulders and cause complications down the line. The insertion site should be kept dry with a plastic covering, if you wish to shower. You will be given instructions on how to care for your PICC if you do some of your treatment at home.

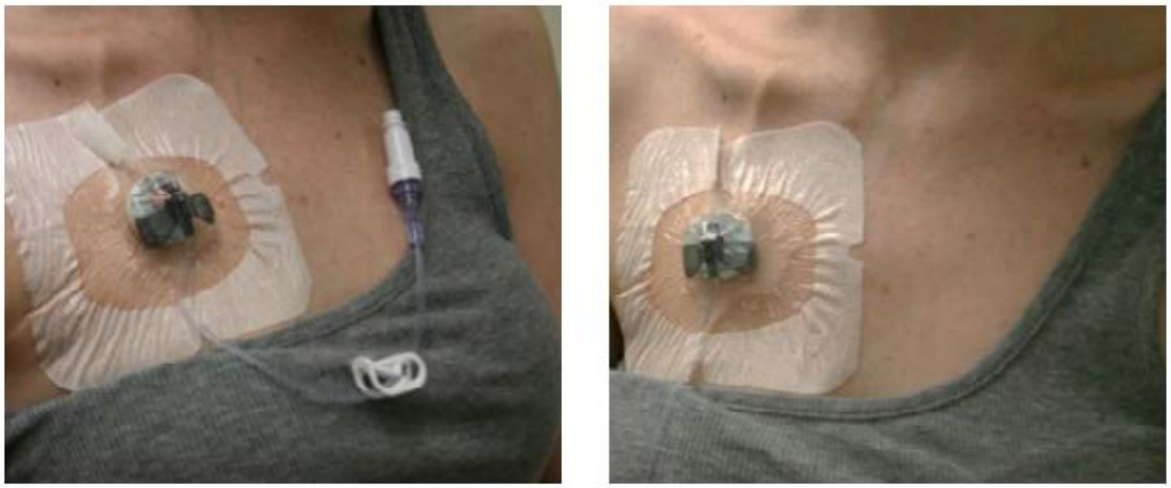
The PICC must be flushed at regular intervals. This means that a small volume of sterile fluid (like saline) in injected into the PICC to keep it flowing nicely. This procedure must be done in a clean way, using "sterile technique." If you or a family member is unable to flush the PICC properly, a nurse should be available to provide this service.

PORTs (TIVADs)

Ports stay in place even when you are not getting any IV antibiotics. They are hidden beneath the skin with only a small bump to indicate where they are. The procedure to put in a port is more invasive than the approach taken for PICC placement, but it is still quite simple and can be done as an outpatient. Typical positions for ports include the upper chest area just below the collarbone. Less commonly, ports can be placed along the side of the chest wall or inside the upper arm.

Placement of ports is done by a team that is specially trained to do the procedure using sterile technique. The team placing the port (either surgery or radiology) will mildly sedate you, numb the area, make a small incision (about one inch long) and then place the port in a "pocket" beneath the skin surface. Some special care of the site will be needed for a few days while the incision heals and occasionally some pain medication is needed for local discomfort. Once the incision is healed, you will have a bump on the skin and a small scar. If the port needs to be removed for any reason, the incision is re-opened.

To start treatment with IV therapy, the port needs to be accessed. Beneath the skin small well that is about the size of a woman's watch. The "face" of this well contains a rubber septum, which is the access target. A trained professional will swab an antiseptic over the port and then pierce the septum with a special type of needle that has a 90 degree bend, called a Huber needle. Once the needle is placed, it is covered with a sterile dressing and is ready for use to deliver IV antibiotics. During a course of therapy, the Huber needle and dressing should be changed every 7 days.



Port accessed with Huber needle. This port is in a common location on the chest wall.

Ports are helpful because their placement under the skin means less maintenance, although you still do need to have the port flushed every 4 weeks, when it is not in use. Once a port has been placed and the small incision is healed, there are no restrictions on activities (such as bathing, swimming, etc.) and most sports (though heavy contact sports like football and hockey should probably be avoided). In general, people with CF decide to get a port when they need frequent courses of IV antibiotics or if they have had a hard time having PICCs placed. Feel free to discuss the decision about whether a port would be best for you with your CF care team.

GET HELP WHEN YOU NEED IT

Managing the upkeep of your VAD is generally simple but should be done regularly and with the help of your care team.

Both PICCs and ports need to be flushed with a sterile fluid like saline (sometimes heparin) after an infusion of medication to prevent the catheter from getting plugged by a blood clot. The frequency of flushing will be up to your care team, but you can expect it to be anywhere from several times a week (for PICCs) to about once per month (for ports). If you are currently receiving IV therapy, you or your nurses will flush after each dose of medicine.

Your VAD should never be painful or uncomfortable to use after a few days following insertion. If it is, notify your CF healthcare team immediately--it could be the beginning of an infection or clot.

Any swelling, puffiness, or redness around your VAD is not normal. Contact the healthcare team if you have fever, chills or other signs of infection (such as any drainage from the catheter insertion site). Your team will need to sort out if your symptoms are related to the VAD or something else. Blood cultures may be ordered as part of the evaluation process.

Contact your team if you experience any of these other problems:

- **Leaking from the catheter or site.** Leaking may mean a hole or break in your tubing--or blockage in the catheter.
- **Blood backing up in your infusion tubing.** This should not happen. If it does, there may be pressure at the catheter tip that can lead to clots.
- **Resistance to flushing.** Feeling resistance may mean that a clot is blocking flow through the catheter. This can often be treated with a clot-busting medication (thrombolytic)

Source: Adapted from Adult Guide to Cystic Fibrosis, Cystic Fibrosis Foundation, 2017.

Lung Transplantation

Referral for lung transplant evaluation has traditionally occurred when the FEV1 percent predicted drops below 30%. Based on improved outcomes post-transplant in the CF population there has been a recent move to evaluate patients earlier (FEV1 percent predicted <40%). Clinical status also has an important bearing. Other factors that figure into timing of referral include need for supplemental oxygen, frequency of hospitalizations, hemoptysis and recurrent pneumothorax.

Criteria for Lung Transplantation

Each transplant center has its own criteria for transplant listing; however, certain criteria are generally accepted:

- End-stage lung disease
- Not responding as well to available standard therapies
- No other chronic medical conditions such as heart, liver, or kidney disease
- No recent cancer (usually need to be cancer-free for $\geq$ 5 years, except for skin cancer)
- Absence of certain infections: HIV, hepatitis and certain bacterial/mycobacterial infections. Most centers will not list patients harboring *Burkholderia cenocepacia or B. dolosa*
- No active alcohol, drug or tobacco use
- Acceptable body mass index (some require BMI $\geq$ 18)
- Acceptable psychological profile
- Adequate social support system
- Ability to adhere to a complex post-transplant regimen and treatment recommendations

Pre-Transplant Evaluation

Pre-transplant evaluation is a deliberate process that works best in the outpatient setting. This is typically NOT initiated when a patient is acutely ill, and transfer of inpatients to a transplant center for urgent evaluation is almost never done. The evaluation involves an extensive series of medical tests and interviews to assess suitability for transplant surgery and post-surgical success. Testing outside usually lab studies generally includes the following (though this is not all-inclusive and some centers have different requirements):

- Blood typing: Blood type must match the donor
- Tissue typing: Ideally, recipient tissue should match that of the donor, but the closeness of the match must be balanced against the urgency of need.
- CT scan of the chest
- Pulmonary function testing

- Oxygen assessment with arterial blood gas and 6 minute walk distance test
- Bone density (DEXA) scan
- Cardiac stress test and blood pool scan
- Cardiac catheterization (may include both right and left heart procedures)
- Electrocardiogram
- Ventilation/perfusion scan
- Echocardiogram
- 24 hour pH probe test for acid reflux
- Sinus CT scan
- Vaccinations: influenza, hepatitis A/B, pneumococcal, and tetanus
- Dental check
- Cancer screen (for example, gynecological exam, colonoscopy, mammogram)

The evaluation also involves meeting with members of the transplant team, including the following: social worker, financial coordinator, dietitian, physical therapist, respiratory therapist. The evaluation may also involve meeting with psychiatrist/psychologist, anesthesiologist, infectious disease specialist or hematologist. This team should work in concert with the local CF team to determine where each test or evaluation would be best performed.

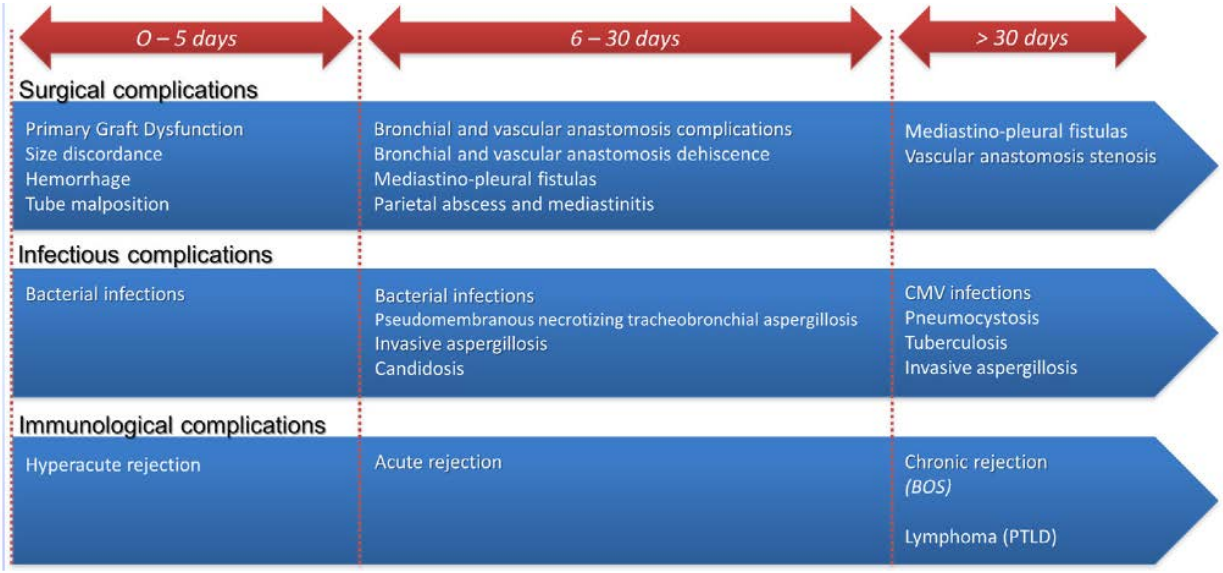
On the Transplant List

Once approved by the transplant team, patients are put on a regional waiting list. The average wait time varies considerably by center and patient characteristics and can rarely be accurately predicted for an individual. The position on the list is determined by the Lung Allocation Score (LAS). The LAS system looks at severity of lung disease and ranges from 0 (mild) to 100 (most severe). Scores are typically recalculated every 6 months but may be checked with any change in clinical status. This period of waiting on the list can be a frustrating time, and it is very important for patients to avail themselves of support from the local CF team, transplant team, family, spiritual care providers and rehab specialists in order to maintain life balance.

Transplant and Beyond

CF patients ALWAYS undergo bilateral lung transplant (transplant of both the right and the left lung), since it is not beneficial to leave any original, infected lung tissue in the chest. Transplant teams work very hard to get patients off mechanical ventilation as soon as possible after the procedure. Potent immunosuppressant medication is started a couple of hours before surgery to prevent acute graft rejection. Medications include the following: induction agents (monoclonal agents like basiliximab or polyclonal agents like anti-thymocyte globulin); calcineurin inhibitors (tacrolimus , cyclosporine) and antiproliferative agents (mycophenolate, azathioprine, corticosteroids or--less commonly--sirolimus). Since medications are used to suppress the immune system, patients are susceptible to infection. In the immediate

perioperative period, patients are treated with intravenous antibiotics and antifungal therapy based on most recent sputum culture results. Prophylaxis against *Pneumocystis jiruveci* (PJP) is started right after surgery and many patients are also treated with antiviral therapy and antifungal therapy. The Figure shows the most common timing of various post transplant complications. Generally after transplantation, patients are followed very closely for the first year by the transplant center. Therefore, patients coming to Maine Medical Center with pulmonary complications more than a year after the procedure will be seen for infectious or immunological disorders. If chronic rejection (obliterative bronchiolitis or BOS) is in the differential diagnosis, then a non-contrast chest CT with inspiratory and expiratory views should be considered along with pulmonary function testing. If infection is in the differential diagnosis, then there should be a low threshold for bronchoscopy. Lung nodules may be related to infection or to post-transplant lymphoproliferative disease (PTLD). Pulmonary consultation should always be obtained and close communication with the transplant center ensured in patients who are post lung transplant.



From Hemmert C. et al. Diag Interv Imaging, 2014. 95: 399-409.

Critical Care

Consideration for transfer of a CF patient to a critical care bed is a relatively rare event. Nonetheless, it is worthwhile to review the circumstances where such a decision arises and the Adult CF Program positions on various scenarios that involve critical care services. Emphasis is on aggressive, early interventions to maximize effective airway clearance, preservation of functional (ambulatory) status, and rapid liberation from mechanical ventilation. In general patients who have a Do Not Resuscitate (DNR) status should be not be admitted to the intensive care unit for respiratory failure. This may require difficult and sensitive conversation(s) among members of the CF team and the patient and his/her family.

ADMISSION CRITERIA

Acute respiratory failure or requirement for intense airway clearance treatment not manageable in IMC, or other acute ICU level healthcare need. Occasionally, patients will require transfer to ICU for medication desensitization (covered in another section) or general medical emergencies.

MANAGEMENT OF RESPIRATORY FAILURE

- Non-invasive positive pressure ventilation (NPPV) or high flow nasal cannula (HFNC) should be used for respiratory muscle rest at night and with naps. The choice of modality should be based on physiologic requirements and ability of the patient to comfortably interface with the assistive device.
- Chest physical therapy (PT) for secretion clearance is not effective if done while the patient is actually on NPPV, so PT sessions will be done when the patient is off NPPV. The goal should be to have the patient off NPPV between 09:00 and 16:00 (exception for naps and respiratory muscle fatigue) to allow sufficient time for effective chest PT and inhalation treatments.
- When a patient cannot be liberated from NPPV long enough to complete airway clearance and inhaled medications, it will be considered a “failed day” (reflects a day in which secretion clearance modalities are ineffective). During a "failed day", patients may actually appear to stabilize temporarily only to deteriorate 1-2 days later following mucus impaction from continuous positive pressure ventilation.
- Respiratory therapy (RT) may suggest use of a MetaNeb® device to help with airway clearance. Some patients may benefit but, again, frequent use of this device may lead to the same problems as NPPV.
- Consider addition of systemic steroids (10-60 mg Prednisone equivalent daily), particularly in patients with a history of elevated IgE or reactive airways disease. Steroids may also assist in the short term with anorexia, musculoskeletal pain, pruritus and overall sense of well being. Watch for hyperglycemia, which can be extreme in this population.
- Consider infectious disease consultation, and ID pharmacy assistance to ensure adequate coverage and dosing. CF patients with advanced lung disease often harbor unusual, multidrug

resistant organisms and pharmacokinetics and pharmacodynamics of many medications are altered in CF.

- Consider palliative care consultation. Some of the patients may have a relationship with this team from the outpatient setting.

Intubation: Two back-to-back "failed days" will be considered a flag for intubation. This will trigger a face-to-face meeting with the patient and family by the attending to discuss intubation and plan or care. Please contact the on call Adult CF Program physician if intubation is anticipated (on call physician is listed in Amion). In general, it is not possible to do the transplant listing process for patients on a ventilator and therefore patients with end stage lung disease who have not been previously evaluated should usually not be intubated. Patients who have progressive respiratory failure should receive comfort care when not candidates for intubation.

1st intubation day:

- All reasonable modalities to promote airway clearance and improve gas exchange should be considered (e.g., chest PT, high frequency oscillator vest use, flexible bronchoscopy for mucus plug clearance; prone positioning). Patients may require multiple sessions daily of each of these. The oscillator vest can be left in place on the patient to facilitate multiple sessions overnight
  - **Note:** prone positioning is being used for airway clearance, not specifically for hypoxemia, so prolonged periods are not necessary
  - CF patients typically lack subcutaneous fat; special care may be needed to protect bony prominences.
  - Consider timing of different modalities (e.g., bronchoscopy immediately after oscillator vest treatments, or during proning)
- Anticipate a very busy day for physician, nursing (should be "specialed" 1:1), respiratory therapy, and physical therapy.
- It is crucial to continue to provide all inhaled during mechanical ventilation
- If the patient is hemodynamically stable, consider a chest CT as part of a secondary survey (routine or CT angiogram), as often these patients have had limited chest imaging prior to ICU transfer. Potential findings would be loculated pleural effusion, mucus impaction, loculated pneumothorax, cavitary pneumonia, pulmonary embolism, vascular stricture complicating central venous catheter placement.

2nd intubation day:

- Assess effectiveness of various modalities tried on day 1; discontinue those that have not been effective (chest PT and vest to remain regardless)
- Consider alternate modes of ventilation to optimize synchrony with the ventilator and gas exchange. Generally, permissive hypercapnia is employed to minimize barotrauma and volutrauma during mechanical ventilation. Suppress fever and avoid overfeeding in this context. Judicious use of neuromuscular blockade may be needed.

- Slow bowel motility can be a major problem in bedridden CF patients, especially those who are receiving narcotic medications. Abdominal distension should be considered during evaluation of abdominal pain, nausea, emesis, agitation, and ventilator dyssynchrony. Distal intestinal obstruction syndrome (DIOS) is characterized by a palpable fecal mass in the right lower quadrant. Usually a plain abdominal film can confirm the diagnosis. Pre-emptive use of osmotic agents such polyethylene glycol via orogastric or gastrostomy tube may prevent the need for surgical evaluation. Abdominal CT scan with enteral and IV contrast can be diagnostic and therapeutic (diaztrizoate [Gastrografin®] is an osmotic agent) in challenging cases.
- If extracorporeal membrane oxygenation (ECMO) being considered, there must be contact with transplant center willing to accept patient on ECMO. The on call CF physician should be involved in this consideration and will be able to facilitate communication with the transplant center under these circumstances. Designated members of the medical critical care, cardiovascular critical care, and perfusion teams should be contacted to evaluate the appropriateness of ECMO and right-fit the circuit to the patient.

Tracheostomy

- Should be the expectation on intubation day 3, barring dramatic improvement and anticipated extubation within next 24 hours. The decision to move toward tracheostomy should not be viewed or presented as a clear sign of failure, but, rather, as choice to promote early lightening of sedation and mobilization. Immobilization results in inactivation from lung transplant listing at most centers.
- The plan should be to initiate ambulation on full vent support, and this requires careful coordination between nursing, respiratory therapy, and physical therapy staff.

Nutritional Support

- A percutaneous gastrostomy tube (PEG) should be placed at same time as tracheostomy (if the patient does not have a PEG). Even a few days without nutrition can lead to significant weight loss in this patient group. Consider placement of a percutaneous gastrostomy-jejunostomy (PEG-J) tube in those patients with a history of clinically significant reflux.
- Tube feeds may need to adjusted based on nutritional status and ventilatory mode (e.g., bolus tube feeds may not be appropriate with prone ventilation schedule).
- Administration of pancreatic enzymes can be problematic in mechanically ventilated patients. Most pancreatic enzyme formulations (either microcapsules or microtablets) will gum up feeding tubes. Work with the inpatient nutrition team, CF team and pharmacy to troubleshoot this issue. A device called the Rilizorb™, a digestive enzyme cartridge containing immobilized lipase, can be placed in line with the tube feeding pump to improve nutrient absorption in pancreatic insufficient patients.
- Calorimetry should usually be done by day 4, as long as the patient does not harbor MRSA.

Weaning

- Need to be cognizant of potential for over-fatigue with wean and rehab activities.

- CF patients are particularly vulnerable to sudden decompensation due to mucus plugging. Meticulous attention to airway clearance is important
- For patients with intercostal muscle strain or rib fractures, analgesic medication may be necessary to allow chest physical therapy. Transdermal lidocaine and non-narcotic analgesics may be helpful adjuncts to narcotic medications
- Team meeting to determine appropriate schedule for chest PT/vest, vent weaning, ambulation sessions; schedule should be posted in the room.
- Again, consider alternative vent modes/wean strategies as better suited to patient tolerance/comfort (PCV, PSV). May be able to use portable vent.

SOCIAL WORK

- The CF social work team can play a valuable role in this population, assisting the critical care social work staff with family support and clarification of financial issues.
- The social work team is also available to communicate with their professional contacts at transplant centers, as needed.

MISCELLANEOUS

- Obtain a manipulative medicine consult, if not already in place
- Offer chaplain involvement to patient and family
- Involve patient to the extent possible at every stage (i.e., not just for consent for intubation, but also for input around activity schedule, sleep-wake times, etc.)
- Engage the CF team. The expectation is for daily contact between the CF attending the SCU attending, as appropriate

Carefully coordinate transfers to the transplant center. The Adult CF Program has resources to help in this process: Program Coordinator, Alicia Murry; Medical Assistant, Kim Jackson; Social Worker, Simon Macdonald. Usually initial contact with the transplant center will be made by the on call CF attending (see Amion) with direct communication to patient/family, SCU team.

Topics in Antimicrobial Therapy

Protocol for early eradication of *Pseudomonas aeruginosa*

MAINE MEDICAL CENTER ADULT CF PROGRAM

Eligible Patients:

- First infection with *Pseudomonas aeruginosa*
- New infection with *Pseudomonas aeruginosa:* new isolate following bacterial clearance documented by 4 negative cultures in the previous 1-2 years

Contraindications:

- Allergy to tobramycin* or ciprofloxacin
- Hearing loss, loop diuretic use, other contraindications to tobramycin
- Infection with other resistant gram negative organism
- Recent use of chronic azithromycin (within 1 month)
- Acute exacerbation or other intercurrent health issue

Protocol

- Start ciprofloxacin 500-750 mg by mouth every 8-12 hours x 28 days
- Start tobramycin inhaled 300 mg every 12 hours x 28 days
- Obtain repeat sputum culture at 1 month, 2 months, and then return to standard culture with each visit (goal of 4 sputum specimens in the year following eradication)

Data suggest that this should result in an eradication rate of approximately 60-65%, with a 5-10% adverse effect rate requiring discontinuation (nausea, vomiting, wheezing, exacerbation). There is no U.S. data proving that eradication improves long term outcomes at this time. There is a suggestion that this may be the right approach based on the European experience.

Sources

Taccetti G, Early antibiotic treatment for Pseudomonas aeruginosa eradication in patients with cystic fibrosis: a randomised multicentre study comparing two different protocols. Thorax. 2012 Oct;67(10):853-9.

Ratjen F, et al. Treatment of early Pseudomonas aeruginosa infection in patients with cystic fibrosis: the ELITE trial. Thorax. 2010 Apr;65(4):286-91.

Langton Hewer SC, Smyth AR. Antibiotic strategies for eradicating Pseudomonas aeruginosa in people with cystic fibrosis. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD0041

IV Antibiotic Desensitization: Adverse Reactions

If symptoms develop during the desensitization procedure, the infusion should be temporarily halted until symptoms have resolved. On some occasions, symptoms may resolve with cessation of the infusion alone. Contact the supervising provider for ANY severe or prolonged reaction, or any questions regarding the protocol, reactions, and appropriate management. Desensitization should be aborted if a patient develops hypotension and/or laryngeal edema that is not immediately responsive to IM epinephrine.

Severity	Manifestations	Management
MILD*	• Isolated itching • Flushing • Mild urticarial (hives) • Nausea • Abdominal pain • Back pain	• Stop current infusion and watch for symptom resolution • **DO NOT** immediately give rescue meds • After the reaction subsides: -*Adjust Pump* – infuse at slower rate (i.e., double infusion length to 30 min) -*Resume protocol* – repeat the step at which the reaction occurred, using the new prolonged infusion rate • <u>Subsequent reactions</u> – If patient still reacts over the prolonged infusion: -*Stop infusion* and discard dose -*Go back* to previously tolerated dose -*Infuse* previously tolerated dose and all subsequent doses over prolonged rate -*Notify* provider on call
MODERATE*	• Coughing/wheezing • Chest tightness • Shortness of breath • Diffuse hives	• **Stop infusion** and immediately notify provider • *Consider* inhaled bronchodilators/O_2 • *Consider* IV antihistamines • *Proceed* per provider discretion
SEVERE	• Laryngeal symptoms (stridor, throat swelling) • Wheezing/↓ O_2 sats • Hypotension	• **Stop infusion** and immediately notify provider • *Call* rapid response team to bedside • *Administer* (1:1000) 0.3 mL IM followed by diphenhydramine 50 mg IV x 1 • *Abort* desensitization procedure

*Without hemodynamic instability and/or airway compromise

<u>Rescue medications:</u> (should be at bedside prior to starting protocol)

- Epinephrine (1:1000) 0.3 mL IM PRN
- Diphenhydramine 50 mg IV infusion (over 2-5 min)
- Hydrocortisone 100 mg IV push

Pharmacy Contacts	
SCU Pharmacist	Phone: 662-7980
IV Room	Phone: 662-4113
Verification Room	Phone: 662-2801
STAT Line	Phone: 662-3333

MILD REACTIONS

Mild reactions include urticaria (a red skin eruption characterized by round, red areas of swelling) and pruritus (itching) that arise during the procedure. In that event, the following is recommended:

- **Stop current infusion** and watch for symptom resolution
- **DO NOT** immediately administer antidote medications
- Consider diphenhydramine 50mg IV x 1 dose at the discretion of the provider. Antihistamines should be considered in the setting of worsening urticaria and pruritus, or if symptoms do not spontaneously resolve after the infusion has been temporarily stopped.
- Consult with provider on call for further instructions.

<u>After the reaction subsides:</u>

- **Adjust pump** - infuse at slower rate (i.e., double infusion length to 30 min if previously infusing over 15 min)
- **Resume protocol** - repeat the step at which the reaction occurred using the prolonged infusion rate

<u>Subsequent reactions</u> - If the patient still reacts over the prolonged infusion:

- **Stop infusion** and discard dose
- Go back to previously tolerated dose
- Infuse previously tolerated dose and all subsequent doses using the prolonged infusion rate
- Inform the provider on call
- Clearly document in the patient's chart any reactions that develop, including:
  -Patient's symptoms, vital signs, and physical findings
  -Exactly when the reaction occurred (i.e., how many minutes into a particular step)
  -How and when the reaction resolved and any treatments administered

MODERATE REACTIONS

Moderate reactions include coughing,wheezing, and/or chest tightness that arise during the procedure. In that event, the following is recommended:

- **Stop current infusion** and contact the provider
- Consider diphenhydramine 50mg IV x 1 dose at the discretion of the provider
- Consider administration of supplemental oxygen
- Consider administration of bronchodilator medication
- Consult with provider on call for further instructions
- Clearly document in the patient's chart any reactions that develop, including:
  -Patient's symptoms, vital signs, and physical findings
  -Exactly when the reaction occurred (i.e., how many minutes into a particular step)
  -How and when the reaction resolved and any treatments administered

ANAPHYLACTIC REACTION

Anaphylactic reactions are characterized by hypotension (low blood pressure), mucosal swelling, difficulty swallowing, chest tightness and sometimes rash. In that event, the following is recommended:

- **Stop current infusion, administer oxygen and contact on call provider**
- Call rapid response team to the bedside
- Administer antidote medications:
  -Diphenhydramine 50 mg IV
  -Epinephrine (1:1000) 0.3 mL by intramuscular injection (IM)Consider administration of bronchodilator medication
  -Inhaled bronchodilators
- Consider this a *desensitization failure*

- Clearly document in the patient's chart any reactions that develop, including:
  a. Patient's symptoms, vital signs, and physical findings
  b. Exactly when the reaction occurred (i.e., how many minutes into a particular step)
  c. How and when the reaction resolved and any treatments administered

Sinus Disease

Nearly all people with CF have some degree of inflammation in the sinuses. Just as the lining of the lungs can become chronically inflamed and infected in the CF, so can the lining of the sinuses. As a result, similar processes occur in the sinuses that can lead to significant and long-term problems. Those people with CF who have sinus symptoms in childhood often have more severe sinus disease as adults and tend to require more sinus attention.

Many treatment options are available to make dealing with sinus issues more bearable. With awareness and attention, you and your CF team can help minimize the effects sinus issues have on your body and your lifestyle.

Learning about your sinuses

The exact purpose of the sinuses is not known, though they are thought to lighten the skull, protect the eyes and brain from injury, and shape the tone of the voice.

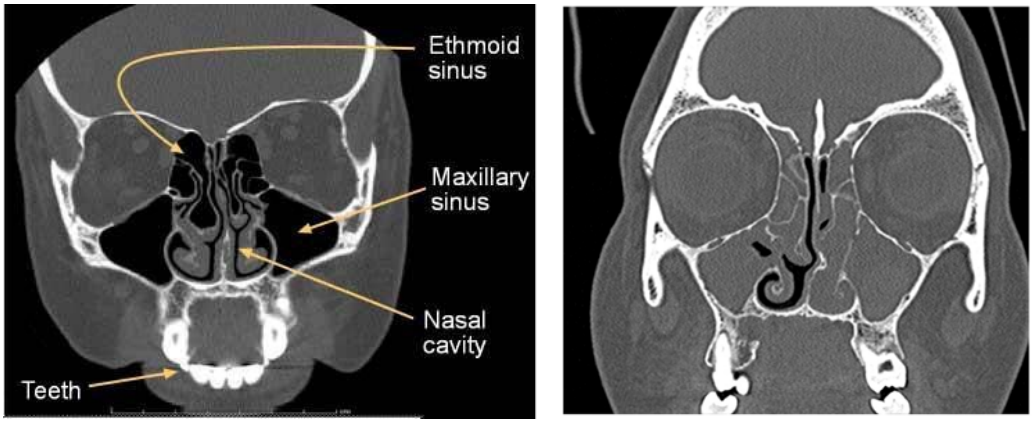
The lining of the sinuses constantly produces mucus. In the normal state, this mucus provides some protection from the external environment. The mucus is swept through small pathways from the sinuses into the nose and throat, where it is generally swallowed or coughed out. When CFTR protein is not functioning well, mucus becomes thick and dry and cannot be swept away. This contributes to chronic inflammation and creates an environment in which bacteria and viruses can grow. Over 50 percent of people with CF have nasal polyps, which are swollen, fluid-filled tissues that grow from the sinuses and can block the nasal passages.

Symptoms of sinus infection and inflammation include discolored nasal discharge, nasal obstruction or blockage, nasal congestion, pressure/pain/headache, decreased sense of smell, and postnasal drip. The term "sinusitis" refers to an infection in the sinuses. In addition to the symptoms noted above, it can also cause fatigue, ear fullness, and cough.

Evaluation of the Sinuses

The sinuses consist of air-filled spaces in the face and skull. They have special names as shown in the illustration: Maxillary (cheek), frontal (forehead), ethmoid (between the eyes), and sphenoid (behind the eyes). At some point, your CF team may order a computed tomography (CT) scan of your sinuses to better understand the extent to which the sinuses are inflamed, how much fluid has accumulated in them, and if polyps are present. You may be referred to an otolaryngologist, head and neck surgeon (ENT), a surgical specialist who deals with disorders of the ears, nose and throat. After asking about your symptoms, the ENT specialist may perform nasal endoscopy using a flexible scope to look up inside the nose to examine for evidence of infection, swelling or blockage. If infection is noted, a sample can be obtained to test for bacteria and guide further care. This procedure is usually quick and simple and can be done in the office. Most of the time, sinus disease can be treated with nasal irrigations, anti-inflammatory sprays and sometimes with antibiotics. Sometimes, particularly if there is ongoing headache, fever or head pressure

related to sinusitis, surgery is recommended. This procedure should be coordinated with the CF team, since IV antibiotics and intensified lung treatments are often used around the time of surgery.



Sinus CT scan from an unaffected individual (left panel), shows well-aerated sinuses as labeled. Notice that the air in the sinuses appears black on the CT image. The sinus CT from a CF patient (right panel) shows diffuse mucosal thickening and loss of aeration.

USE THE RIGHT THERAPIES

Saline Rinses: On a day-to-day basis, clearing out thick mucus can be difficult. Saline (salt water) rinses are helpful to treat allergies, clear out environmental debris such as dust, and mobilize stagnant mucus.

High-volume rinses, either with a Neti Pot or a squeeze bottle, appear to be better than simple sprays. With these techniques, saline goes in one nostril, behind the nasal bone, and drips out the other nostril. It may take some practice getting the technique down, but once you do, it is pretty easy.

Hypertonic saline as a solution that is very salty. It can help reduce swelling and may thin out mucus, but it may cause a burning sensation when rinsing, and the beneficial effects are temporary. Most people with CF prefer regular saline (usually 1-3%), which is just about as salty as normal human tissue. Your CF team will help you get the right kind of saline for your sinuses. Sometimes ENT surgeons or CF care teams recommend rinses with antibiotics that are aimed at specific bacteria that may be affecting your sinuses.

Controlling inflammation: Steroid medications worked to reduce inflammation. Nasal steroid sprays are not absorbed well by the nasal tissue, and daily use should not carry the side effect risks of steroids taken by mouth for many days to weeks. If you have allergies, antihistamines and other anti-inflammatory therapies can also be helpful.

A nice webcast can be found at:
https://www.youtube.com/watch?v=j53imMOPbm8&list=PLhoQ6vyZhgqo3qHxD2lsX6DCqTcinxghE

Source: Adapted from Adult Guide to Cystic Fibrosis, Cystic Fibrosis Foundation, 2017.

Basics of the Digestive Tract

Distal Intestinal Obstruction Syndrome (DIOS)

DEFINITION:

DIOS (formerly called meconium ileus equivalent) is a recurrent, sometimes chronic, partial or complete small bowel obstruction that is unique to patients with CF. DIOS is an obstructive process that starts at the terminal ileum and extends distally. Constipation is an obstructive process that typically starts at the sigmoid and extends proximally. They often occur together, but you don't have to have constipation to have DIOS and vice versa. Patients may have chronic symptoms with exacerbations, or discrete symptom-free periods with acute episodes. Usually there is a variable degree of partial obstruction, but it can become complete.

CLINICAL PRESENTATION:

Symptoms:

- Crampy abdominal pain (often in the right lower quadrant)
- Anorexia
- +/- weight loss
- Flatulence
- Stool pattern may continue to be normal
- +/-vomiting

Signs:

- Tender, distended abdomen. Typically, peritoneal signs are NOT present
- Right lower quadrant mass
- Rectal exam unremarkable (though constipation can occur with DIOS)

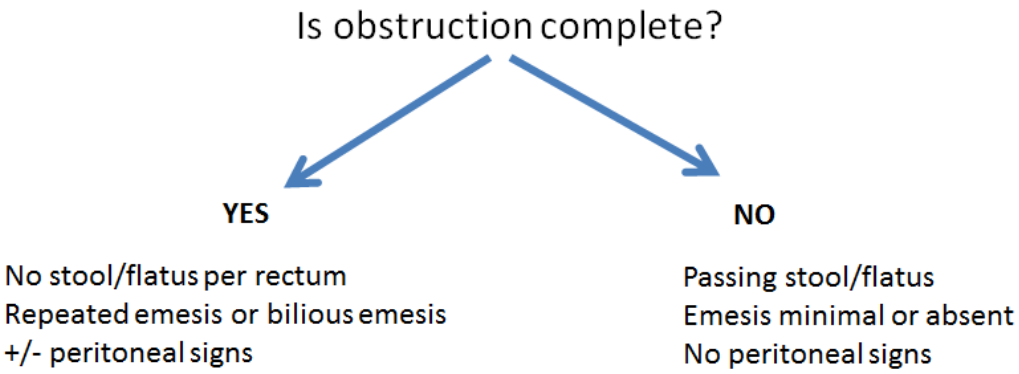
Laboratory Evaluation:

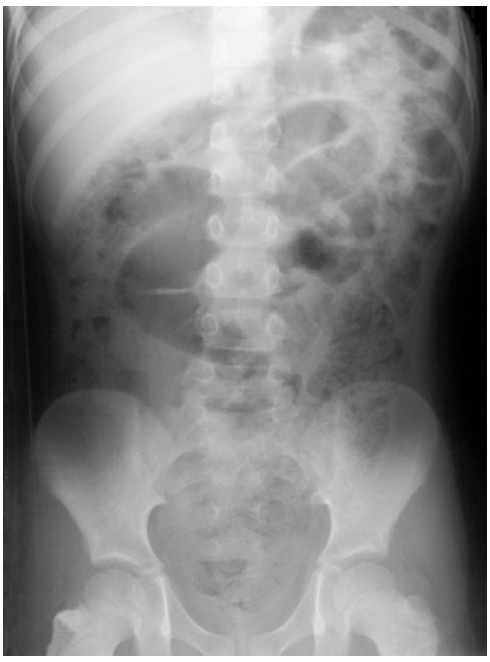
- Supine and upright x-ray (may show bubbly granular material in the right iliac fossa, air fluid levels, and a variable degree of small bowel dilatation)
- Routine labs (CBC, urinalysis, CMP, lactate, pregnancy test). Typically in DIOS there is NOT a lactic acidosis.
- Abdominal and/or pelvic ultrasound and CT scans are used to rule out other causes of abdominal pain
- Contrast enemas (Gastrografin®) are the most specific test and can help to rule out other etiologies, but are not always needed (see below). Inspissated stool seen on reflux of contrast into terminal ileum confirms DIOS

DIFFERENTIAL DIAGNOSIS:

- Constipation
- Appendicitis (especially retrocecal appendicitis)
- Cholecystitis
- Intussusception
- Narcotic related ileus
- Obstruction from adhesions or other mechanical obstruction
- Ectopic pregnancy
- Pancreatitis (rare, as it is NOT seen in pancreatic insufficient patients)

MANAGEMENT OF ACUTE EPISODES:





Abdominal film showing dilated loops of bowel and "bubbly" opacities within the small bowel, especially in the right lower quadrant

Management of patients with complete obstruction:

- Obtain surgical consultation
- Pass nosogastric (NG) tube for decompression
- Obtain IV access and address fluid status
- Do not give polyethylene glycol solution enterally
- Have radiologist give non-barium contrast enema and attempt to reflux contents into the distal ileum. Hyperosmolar agents can be irritating to the colon and may cause fluid shifts. Iso-osmolar agents are equally effective but much more expensive. Large amounts of contrast are usually necessary.
- In the absence of peritoneal irritation, non-barium contrast agents can be repeated twice a day over several days.
- If complete obstruction persists and/or if there is evidence of peritoneal irritation, surgical intervention is warranted. ALWAYS consider other possible diagnoses as a cause of obstruction in patients who fail to respond to therapy for DIOS.

Management of patients with partial obstruction:

- To prevent nausea and bloating, premedicate with:
  - Metoclopramide (Reglan®) 0.1mg/kg PO or IV (max = 15mg)
  - Consider use of ondansetron (Zofran®) 8 mg PO or 4 mg IV
- Make patient NPO and place *small* NG tube or use
- Wait 30 minutes after premedications, then infuse balanced polyethylene glycol solution (GoLYTELY®, NuLYTELY®, etc.) at 20-40cc/kg/hr, max = 1000cc/hr) - 4 liter infusion total (or in infants and toddlers, 4-6 hours). Start at ½ rate for first ½ hour, then increase as tolerated.
- Treatment may be discontinued when the patient passes stool, abdominal pain and bloating disappear, appetite returns, and a previously palpable right lower quadrant mass is no longer present. Passage of clear effluent alone is not an adequate endpoint.
- Upright and supine abdominal x-rays may be helpful in documenting the resolution of DIOS.
- ALWAYS consider other etiologies, if symptoms do not resolve.

Feeding Tubes

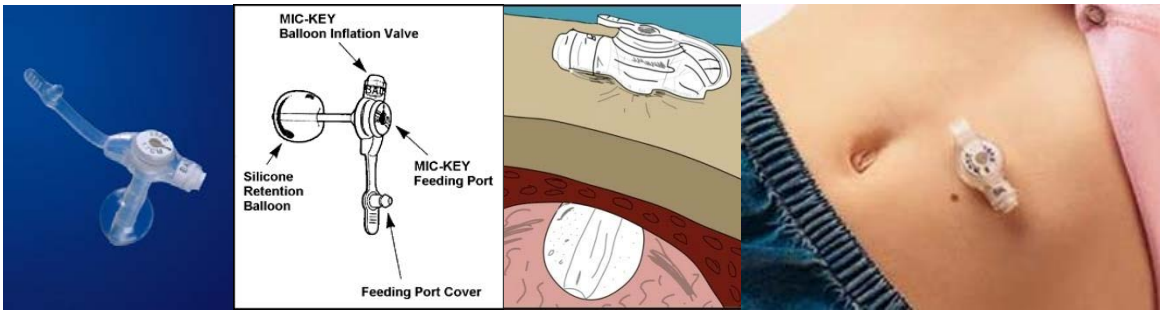
When do I really need a tube?

This section is written mainly for patients but health care staff may also wish to review the material. There are many personal and medical reasons why you may choose to have a feeding tube placed. You may have a goal of wanting to gain weight or just maintain a certain weight. There are many reasons for having healthy weight goals. Good evidence from population-based studies shows that normal ranges of weight and height are associated with better lung function. The Cystic Fibrosis Foundation has established goals for body mass index (BMI) for men (23) and women (22). Your dietitian can explain what weight and caloric intake you would need to achieve to reach your target BMI. In certain circumstances, it may be particularly difficult to approach your target BMI (for instance in the context of poor appetite, nausea/vomiting, or worsening lung function), so consideration of feeding tube placement might be desirable.

What kinds of tubes are there?

Gastrostomy tube (G-tube): The most common feeding tube is a gastrostomy tube, also called a G-tube or a percutaneous endoscopic gastrostomy (PEG) tube. It is a flexible tube that is inserted directly into the stomach through an incision in the abdomen. It makes it possible to deliver nutrition directly into your stomach.

Low Profile "button" G-tube: After a few months of healing from the G-tube placement, your team may recommend replacing the tube with a "button." This device is flatter and lies against the skin of the abdomen. It can easily be placed once the G-tube site is healed, usually about 8-12 weeks after you have had the G-tube placed. At some institutions (like Maine Medical Center), the surgeon may be able to place a low profile "button" G-tube directly. The button can be opened for feedings and closed in between feedings or medications. For many patients, the transition to a button makes tube feedings and care easier and more convenient.



Images of the Mic-Key “button” G-tube. The third panel from the left shows how the retention balloon is inflated in the stomach and serves as an anchor. The right panel shows how this low-profile looks in a patient.

Nasogastric tube (NG tube): An NG tube is a thin, flexible tube that goes in your nose, down

your throat, and into the stomach. This is the least invasive type of feeding tube because inserting an NG tube does not require a surgical incision. These tubes need to be inserted each night and then taken out in the morning for overnight feedings. Most patients are not able to perform this maneuver on a long term basis.

Jejunostomy tube (J-tube): A J-tube is inserted through an incision in the abdomen, directly into the section of the small intestine called the jejunum. It bypasses the stomach. J-tubes are used if a person cannot tolerate feedings directly into the stomach.

Gastrostomy-jejunostomy tube (GJ-tube): A GJ-tube is inserted through the abdomen into the stomach, but it does not stop there. The GJ-tube passes through the stomach into the jejunum to deliver feedings directly into the small intestine, just as they are with a J-tube. This tube is also sometimes utilized when there is excessive acid reflux from the stomach with a G-tube.

NAUSEA AND VOMITING

Possible causes:

- Medications can cause nausea and vomiting
- Something is blocking the intestine
- Tube is not positioned currently
- Tube feeding formula, rate, or amount may not be ideal

What to do

- Reduce the rate of tube feeding
- Space tube feedings farther apart
- If nauseated, hold feedings until the symptoms subside
- Check the amount of liquid you have in your stomach before feeding. This is done with a syringe. Your care team will give you guidelines on when to hold your tube feeding.
- If you feel you will vomit, leave the tube open to drain
- Collier health care professional if nausea and vomiting preventing you from getting your full feedings for more than one day

CONSTIPATION (DECREASE FREQUENCY OR HARD TO PASS STOOLS):

Possible causes:

- Inadequate fluid intake or skipping feedings
- Physical inactivity
- Not enough fiber
- Medications

What to do

- Check that you're taking the prescribed amounts of tube feeding formula and water flushes
- Do not skip feedings
- Participate in physical activity (walking).
- Try 1/2 cup prune juice flushed with 1/2 cup water down the tube one or 2 times per day
- Collier health care professional constipated for more than 3 days

Diarrhea (loose, watery, frequent stools)

Possible causes:

- Tube feeding rate is too fast, (especially if you have a J-tube or small bowel tube was (
- Not enough pancreatic enzymes
- Tube position correctly
- Lack of fiber in diet or tube feeding
- Medications
- Bacterial contamination of feedings, virus, or other infection

What to do:

- Decreased tube feeding rate
- Increase water flushes by 2-3 cups per day to replace losses in the stool
- Keep on use, open formula covered in the refrigerator for only 24 hours, discard if not used
- Use clean techniques restoring getting feedings
- Discontinues laxatives or stool softeners
- Collier health care professional diarrhea it occurs more than 6 times a day

Clogged tube

Possible causes:

- Tube older than 2 years
- Tube has a small diameter or tube that is very long
- Not flushing after tube feedings or medications
- Not dissolving medications well
- Not flushing the tube checking residuals

What to do to prevent a clogged tube:

- Replace old tubes as directed by her doctor
- Flush with only 60 mmol of warm water after feedings, medications, and residual checks
- Do not put any solids or fluids through tube
- Feedings beginning to run and slower, irrigate the tube with water more often

What to do if your tube clogs:

- Push 30 mL warm water through the tube using a pumping motion with syringe (you may need to do this 3-5 times before clog begins to move)
- Try to remove the contents of the tube by pulling and pushing the syringe barrel several times
- Pump air through to the tube using the syringe (you may do need to do this 3-5 times)
- Use small amounts of carbonated beverage to unclog the tube; however, speak with your dietitian or health care professional before using products other than warm water
- Call your health care professional if none of the above methods work to unclog the tube. The tube should flush with some resistance, but you should be able to give feedings, water flushes, and dissolved medicines without difficulty.

Skin irritation around the tube

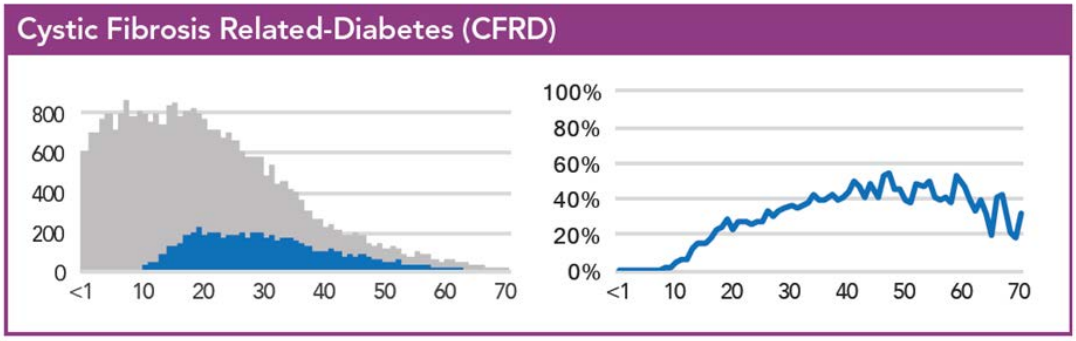
If the area is red and sore, clean it with soap and warm water. Rinse around the area with plain water and dry. You may use an antibiotic ointment around the site. If any areas appear crusty, gently soak or scrub the crusty areas with soap and warm water on the skin and tube itself. If you prefer, you may use a solution of 1:1 hydrogen peroxide and water applied with a cotton swab to clean these areas. After cleaning, rinse with plain water and dry. You may use an antibiotic ointment around the site.

Source: Adapted from Adult Guide to Cystic Fibrosis, Cystic Fibrosis Foundation, 2017.

Improving Nutrition with Tube Feeds

CF-Related Diabetes

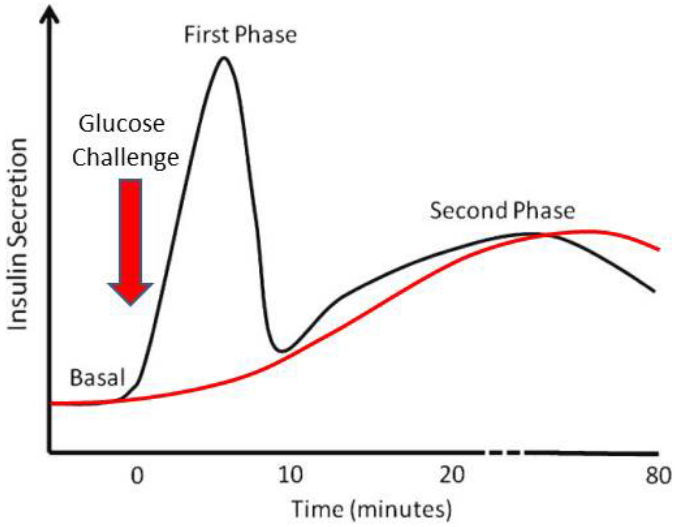
The prevalence of CFRD increases up to about age 50 in the CF population, reaching a peak of 40-50%, as shown in the Figure.



The age related prevalence of CFRD (shown in blue; total population in grey) by numbers in left panel and percentage in right panel. Data is from the 2016 CF Patient Registry.

The most common types of diabetes are type I (insulin-dependent or juvenile-onset) diabetes and type 2 (non-insulin-dependent or adult-onset) diabetes. Insulin is a hormone that lowers blood sugar levels. It also helps cells to take up protein and build muscle in the body. It is therefore known as an *anabolic* hormone. It is made in the beta cells of the pancreas (called the endocrine pancreas). In type 1 diabetes the body stops making insulin. In type 2 diabetes the body lacks normal responses to insulin (most important) and doesn't make enough insulin to control blood glucose levels. CF-related diabetes (CFRD) differs from both type 1 and type 2 in a number of respects (see Table). In patients with CF who take "enzymes" (digestive enzymes are made in a separate part of the pancreas, called the exocrine pancreas) the pancreas develops scar tissue that tends to "choke" the beta cells and reduce insulin secretion. That appears to be why patients who don't need to take enzymes have a lower chance of developing CFRD. Any form of diabetes (type 1, type 2, and CFRD) can lead to the similar symptoms, such as: *polydipsia* (drinking a lot of liquids), *polyuria* (frequent urination), fatigue, unexplained weight loss, and blurred vision.

CFRD is associated with disordered phase 1 insulin secretion from the pancreas, a process that occurs within minutes of a glucose challenge (pre-packaged insulin is simply released). Phase 2 insulin secretion takes more time and is typically delayed in patients with CFRD (see Figure). Both of these problems lead to marked elevation of blood glucose after meals and can sometimes result in HYPOglycemia later on as insulin levels remain elevated and counter-regulatory pathways driven by the liver and pancreas are impaired. Diagnosing diabetes early is important in CF, as studies have shown that diabetes is associated with accelerated decline in lung function. In addition, in the years BEFORE the diagnosis is made there is a trend toward lower body mass and lung function. It is felt that by screening yearly for diabetes, the condition will be controlled before symptoms develop and lead to better overall health.



Cartoon showing abnormal insulin response to glucose challenge in a patient with CFRD (red line) compared to a patient without diabetes (black line). The first phase of insulin secretion is blunted in CFRD.

Characteristic	*Type 1 Diabetes*	*Type 2 Diabetes*	*CFRD*
Onset	Younger	Older	Young adult
Insulin homeostasis	No production	Resistance	Low production Resistance
Diet	Low fat/carbs	Low fat/carbs	Regular diet
Vascular complications	Micro and macro	Micro and macro	Micro

Comparison table for different forms of diabetes

DIAGNOSIS

Diabetes can be diagnosed with a number of tests: Fasting glucose level (a fasting glucose of >126 mg/dL is diagnostic of diabetes); random blood glucose level (a random glucose $\geq$ 200 mg/dL along with symptoms of diabetes, suggests the diagnosis, which would require further testing). Hemoglobin A1c (a level >6.5% is diagnostic of diabetes but a low value does not rule out diabetes). The gold standard test for diagnosing CFRD is the oral glucose tolerance test (OGTT). The test is done as follows:

- Patient must fast for 8 hours
- Blood is drawn to determine the “fasting” glucose level
- Patient then drinks a glucose-containing beverage
- Blood tests are then checked at one and 2 hours after drinking the beverage

Definitions of abnormal OGTT findings:

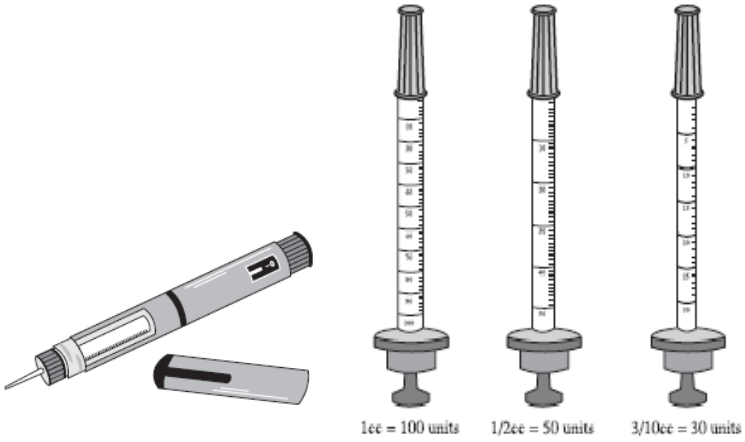
- **Indeterminate Glycemia (INDET)--** A blood glucose level measured in the middle of an OGTT that is at ≥ 200 mg/dL in the presence of normal fasting and 2-hour levels
- **Impaired Fasting Glucose (IFG)--** A fasting glucose that is above normal at 100-125 mg/dL
- **Impaired Glucose Tolerance (IGT)--** A fasting blood glucose of 100-125 mg/dL or a blood glucose 141-199 mg/dL two hours after glucose load
- **CFRD without fasting hyperglycemia**--When the "fasting" glucose is <100 mg/dL but the 2 hour glucose level is ≥ 200 mg/dL
- **CFRD**--Fasting glucose ≥ 100 mg/dL AND 2 hour glucose level ≥ 200 mg/dL

TREATMENT

Since CFRD is primarily related to inadequate insulin production, insulin is the mainstay of therapy. Oral medications (pills) have not been effective for treatment of CFRD. No brand of insulin is better than another, but there are features of each preparation that are important to know. There are also many different types of insulin injection devices. One popular type is the insulin "pen," which is about the size and shape of an ink pen.

Class of Insulin	Onset of Action	Peak	Duration	Generic Name (Brand Name)	Notes
Rapid-acting	15-25 minutes	30-90 minutes	3- 5 hours	Lispro (*Humalog®*) Aspart (*Novalog®*) Glulisine (*Aprida®*)	Covers carbohydrates in meals and snacks. May be taken 5-15 minutes before eating. Used in pumps. One unit of rapid acting insulin will usually lower blood glucose by about 50 mg/dL
Short-acting	30-60 minutes	2-3 hours	6-8 hours	Regular	Covers carbohydrates in meals. Take 30 minutes before eating. May also be used for tube feedings
Intermediate-acting	1-1.5 hours	6-8 hours	12-18 hours	NPH	Covers carbohydrates in meals. May also be used for tube feedings
Long-acting	Glargine: 2 hours Detemir: 3-4 hours	Glargine: No peak Detemir: 6-8 hours	Glargine: 24 hours Detemir: Up to 24 hours	Glargine (*Lantus®*) Detemir (*Levemir®*)	This provides basal insulin. Necessary for all-day insulin needs, but not strong enough to cover carbohydrates with meals

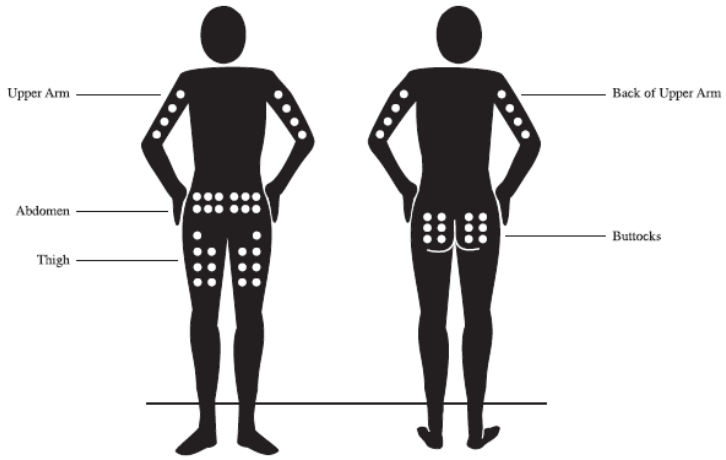
The pen needle is typically 29-33 gauge (the larger the gauge number, the narrower the needle). The insulin is stored in a cartridge inside the pen. A nice feature of the pen is that insulin dosing can be selected by dialing. It is quick, precise and portable.



Cartoons of an insulin "pen" (left) and standard syringe (right)

When using a regular insulin syringe, follow these tips:

- Never mix long-acting insulin in the same syringe as short- or rapid-acting insulin. This will destroy the long-acting insulin
- Clean the injection site with soap and water or alcohol before giving the shot
- Injections may be given in the thigh, buttocks, upper arm or abdominal wall



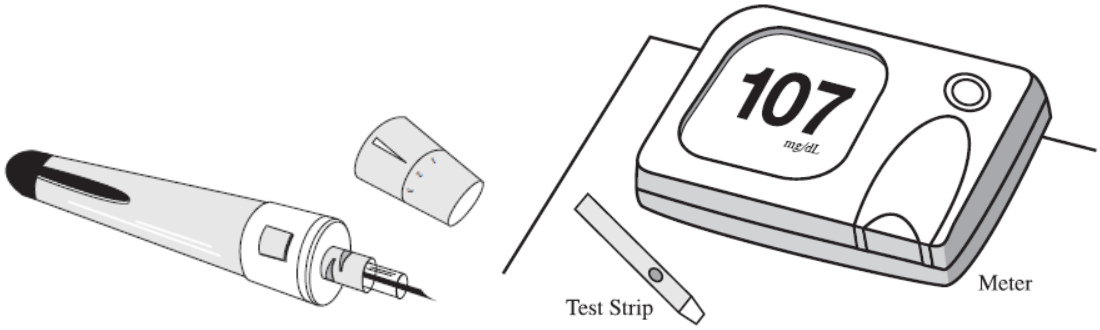
Common insulin injection sites

Patients who struggle with episodic hypoglycemia (low blood sugar), difficulty with highly variable blood glucose levels or who wish to have a ready source of insulin as part of an active lifestyle may benefit from an insulin pump. There are many different models, some of which feature a sensor so that insulin administration is guided by readings from the sensor.

Examples of a stand alone insulin pump (left) and insulin pump featuring a glucose sensor (right)

BLOOD SUGAR TESTING

Blood glucose should generally be checked 3-4 times per day (before meals and at bedtime). There are many types of meters. Most meters are able to store results, which can be very helpful for fine tuning insulin dosing. It is important to always use the appropriate test strips for the chosen meter and to avoid using test strips that are out-of -date. For patients on nighttime tube feedings, blood glucose should be checked prior to starting feeding and 3-4 hours into feeding once or twice per week.



Cartoon of fingerstick lancet, test strip and glucometer

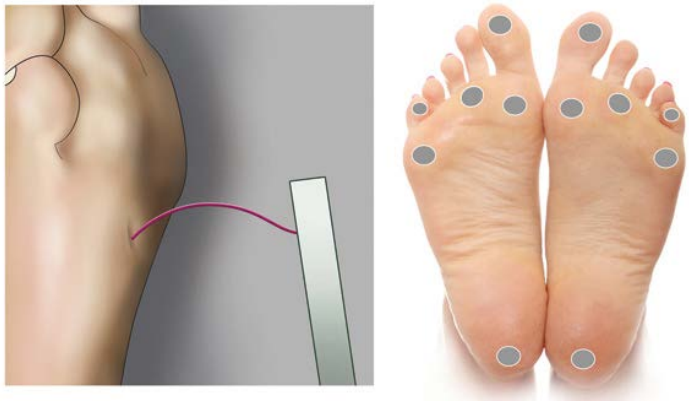
LONG TERM MANAGEMENT

For all patients with CFRD it is important to follow up regularly with an endocrinologist. In addition to labs checked by the primary CF team, these tests will often be performed:

- *Glycated hemoglobin (HbA1c).* This blood test shows how much glucose is "stuck" to hemoglobin in the blood cells. The higher the average blood sugar, the higher the HbA1c. The recommended HbA1c for adults with diabetes is <7%. Normally, red blood cells live for about 3 months, so the HbA1c gives an estimate of glucose control over the previous 3 months . In CF, however, red

blood cells tend to have a shorter lifespan, which can artificially LOWER the HbA1c. This test can still be used to track blood glucose over time but the fingerstick blood glucose measurement is a more precise test of actual blood sugar levels.

- *Fructosamine.* This blood test evaluates the glycation of proteins in the bloodstream. The protein measured in this test is albumin. Since albumin doesn't last as long in the bloodstream as blood cells do, the fructosamine test gives a shorter "snapshot" of blood glucose control over a 1-2 week timeframe.
- *Urine microalbumin.* Uncontrolled diabetes can lead to kidney damage. When the kidneys are injured, more protein spills into the urine (often patients will note "foaming" of the urine when a lot of protein is present). Medications like angiotensin converting enzyme inhibitors (ACEI) may be used to protect the kidneys, if protein is found on repeated tests.
- *Lipid profile.* Blood lipids consist of cholesterol and triglycerides. People with type I and 2 diabetes are at increased risk for strokes and heart disease, particularly if lipid levels are elevated. CF patients who need to take enzymes, seem to have a very LOW risk of developing stroke and heart disease because lipid levels tend to be very low. However, certain patients (such as those who are post organ transplant, have a strong family history of cardiovascular disease, etc.) may benefit from testing.
- *Foot exam.* Nerve damage from diabetes (neuropathy) can occur, especially in those with poorly controlled blood glucose. Sensation can be tested with a tool called a monofilament on the tops (dorsum) and soles (plantar surface) of the feet.



Monofilament testing for neuropathy. The cartoon shows areas that are checked with the fine nylon filament
https://bpac.org.nz/BPJ/2010/October/img/diabetic_foot.jpg

- *Ophthalmology (eye) exam.* In 10-23% of people with CFRD, changes in the retina (or the "film" part of the eye, if we think of the eye like a camera) can occur over time. This is particularly the case for patients with poor glucose control. Retinal damage, or *retinopathy*, can cause blurred vision at first and eventually blindness if blood glucose is not controlled. A yearly eye exam by a an ophthalmologist (rather than an optometrist) is recommended.

HYPOGLYCEMIA (LOW BLOOD SUGAR)

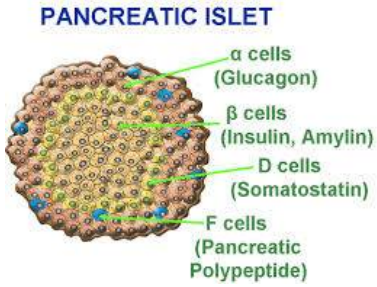
Hypoglycemia is generally defined as a blood glucose <70 mg/dL. Often the body will give warning signs when the blood sugar is going too low in the following ways:

- Sudden hunger
- Nausea
- Shaky feeling hands or body

- “Cold” sweat
- Weakness
- Headache
- Confusion
- Blurred or double vision
- Fast heart beat, palpitations
- Numbness or tingling of the lips
- Emotional change (acting angry, tearful, nervous)
- Loss of consciousness (pass out), seizure (convulsions)-- associated with very low glucose level

NOTE: Warning signs vary from person to person and some patients may not be aware of any these symptoms, particularly as hypoglycemia becomes more severe.

Blood glucose levels are usually tightly controlled by a number of behaviors and hormones in the body. Insulin helps to lower the blood glucose but a number of other hormones serve to balance the insulin effect (“counter-regulatory” hormones). Some of the counter-regulatory hormones, namely glucagon, are made and secreted from the pancreas. In CF, counter-regulatory hormone release may be delayed and/or diminished, raising the risk of hypoglycemia. Other factors that can increase the risk of hypoglycemia include missed meals, extra exercise, excess insulin dose, drinking alcohol, insulin injection into muscle instead of the skin. Patients with milder forms of abnormal glucose handling such as impaired glucose tolerance seem to be at increased risk of developing hypoglycemia, particularly if insulin therapy is instituted. Therefore, the standard recommendation for these patients is to try to control blood glucose levels with small, frequent meals and avoidance of concentrated sweets.



Cartoon of the pancreatic islet showing different cells that are responsible for the production and secretion of insulin and other hormones.

Source: Brunzell, C, Hardin, DS, Kogler, A, Moran, A, Schindler, T. Managing Cystic Fibrosis-Related Diabetes: An Instruction Guide for Patients and Families (6th Edition). Cystic Fibrosis Foundation, 2015.

Basics of Infection Control for Patients

WHY ARE PEOPLE WITH CF MORE SUSCEPTIBLE TO GERMS?

A gene mutation causes a problem with the CFTR protein (see other sections for a more detailed explanation). This protein helps the body move fluids in and out of cells. This movement helps regulate the fluids for digestion, sweat and mucus. When CFTR is not working correctly, the mucus in your lungs does not contain enough fluid to flow normally out of the body. In CF, this is what causes the mucus to become thick and sticky. This thick mucus then interrupts one of the normal ways that the lungs stay clean. The mucus then weighs down and tangles with cilia, hair-like extensions on cells in the nose and lungs that normally trap and sweep away dirt and germs from the airways of the lungs. So the mucus, combined with the interruption of the cilia's job of cleaning, creates a perfect environment for germs to thrive and grow, leading to infection. Infections that develop in this environment become chronic (long-lasting). As the germs multiply, the body tries to fight the infection by sending white blood cells to the scene. This battle, marked by white cells and all of the chemicals they stimulate, is technically called "inflammation." Inflammation and chronic infections lead to scarring and changes in the shape of the airways (technically called "bronchiectasis"). This process repeats itself in CF and is called the "vicious cycle" of infection and inflammation. Unfortunately, bacterial infections are the major cause of lung health getting worse in people with CF. At this time, the best available therapy is prevention or infection control.

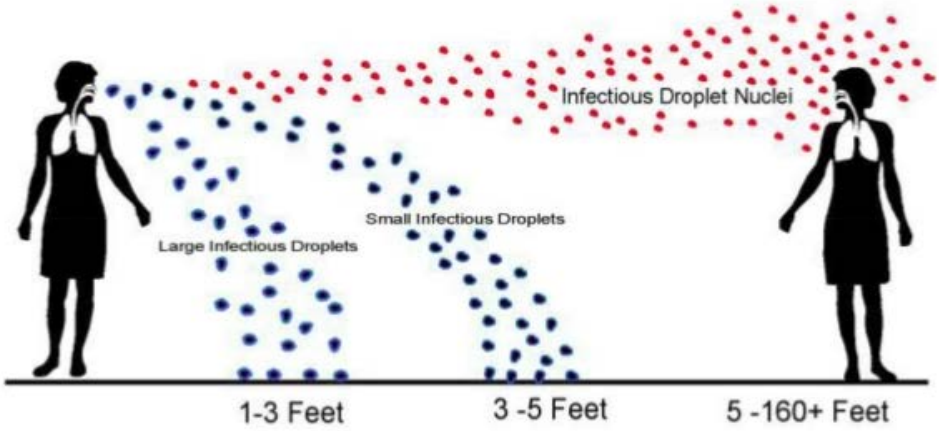
HOW DO I COME IN CONTACT WITH GERMS IN THE FIRST PLACE?

There are three main ways that germs are picked up: through contact, through droplets, and by airborne transmission. The two ways that are of most concern in CF are contact and droplet spread. Most of the germs of concern originally come from soil and water. These germs thrive in moist environments and it turns out that CF sputum is a good home for many of them. In fact important CF *germs can live for hours to days* in sputum on environmental surfaces like countertops or keyboards.

- **Contact transmission** is the most frequent way that germs spread. It includes both direct contact and indirect contact. Common germs that are spread through contact transmission include *Pseudomonas aeruginosa* and *Burkholderia cepacia* complex.

https://i2.wp.com/gbengaadebayo.com/wp-content/uploads/2011/07/germs-on-hand.jpg

- **Droplet transmission** is when germs are passed short distances through coughing, sneezing, or talking. An example of a germ spread by droplets is seasonal influenza ("flu").
- **Airborne transmission** is when germs are carried through the air on dust particles (droplet nuclei) and are inhaled. Tuberculosis and *Aspergillus* (a mold) are spread this way.



Cartoon showing typical distances traveled by droplets (generally ≥ 5 microns diameter) and droplet nuclei (generally < 5 microns) from the source.

Adapted from: https://www.google.com/search?biw=1920&bih=887&tbm=isch&sa=1&ei=KjSEWv-GEcO0jwTqqq-gBg&q=droplet+nuclei&oq=droplet+nuclei&gs_l=psy-ab.3..0l3j0i24k1l7.1163362.1169018.0.1169505.20.14.2.4.4.0.236.1802.0j12j1.14.0....0...1c.1.64.psy-ab..0.19.1994.0..0i67k1j0i5i30k1j0i8i30k1.113.EQxUiqJ5zcQ#imgrc=wKzSUBDAQ5tApM:&spf=1518614716690

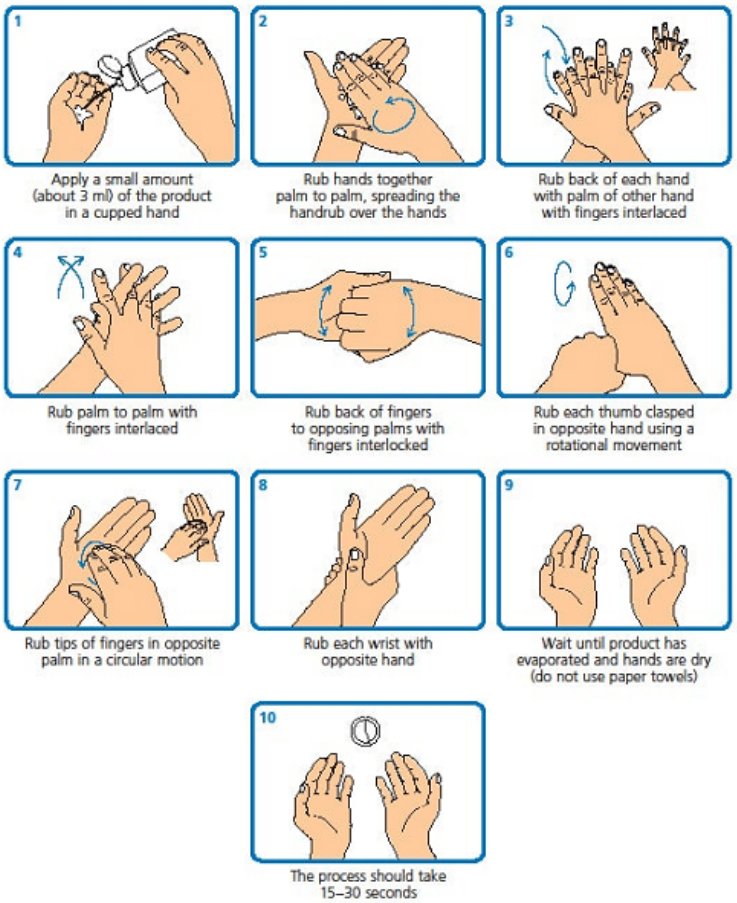
I HAVE A MULTIPLE-DRUG-RESISTANT ORGANISM. WHAT DOES THAT MEAN?

Multiple-drug-resistant organisms (MDRO) in CF are bacteria that have become resistant to multiple types of antibiotics. Resistance means that a particular antibiotic does not work to kill or weaken the bacteria. Some bacteria are naturally resistant to antibiotics. For others, resistance happens when the bacteria is exposed to antibiotics repeatedly over time. With each exposure, the groups of bacteria can adapt to "outsmart" antibiotics or undergo a process called "natural selection" where those bacteria that can resist the antibiotic then go on to multiply, leading to more resistant germs. Patients can also acquire MDRO by coming into contact with a person infected with the resistant germ or equipment that has been contaminated (has the germ on it). Drug-resistant bacteria can be particular problem in CF, as they can make treating your lung infections and exacerbations more difficult. This raises an important point: the misuse of antibiotics is one of the leading causes of antibiotic resistance.

HANDWASHING

Handwashing is a cornerstone of effective infection control for the reasons outlined above. Handwashing may be done either with soap and water technique or with an alcohol-based formulation. Cleaning with alcohol-based hand rub is simpler for people on the go, particularly when there is not ready access to running water. Note, there are two circumstances when the soap-and-water method should be done rather than the alcohol-based method:

- Visibly dirty hands
- When there is concern about gastrointestinal tract infection with *Clostridium difficile* ("C-diff") or norovirus



Cartoons of soap-and-water (top panel) and alcohol-based (bottom panel) hand washing techniques
https://cdifffoundation.files.wordpress.com/2013/06/handwashingii.jpg
https://www.whatdotheyknow.com/request/21723/response/53031/attach/html/2/foiextract20121024-16446-oteuvy-0-26_1.jpg

INFECTION CONTROL IN DAILY LIFE

Hands should be cleaned:

- Before, during and after preparing food
- Before eating food
- After using the bathroom
- After changing diapers or cleaning up a child who has used the bathroom
- After blowing the nose, coughing or sneezing
- Before and after using inhaled medications and performing airway clearance
- Before and after caring for someone who is sick
- After touching an animal or animal waste
- After touching garbage
- Before and after treating a cut or wound

USE OF MASKS

Masks can be used to protect the wearer from germs in the environment (*"inward"* protection) or those around the wearer who might otherwise come in contact with germs (*"outward"* protection). It is known that wearing a mask can be physically uncomfortable (feels harder to breath, "hot", "stuffy", "itchy", promoting more cough, etc.) and also stigmatizing (feeling like an outsider). Therefore, it is really important to know when masks should be worn. When does the benefit of wearing a mask outweigh the negatives? We now have information about this and the policies around mask wearing in clinic and in the hospital are based on what we know from studies. Recent studies have shown that in CF patients, a plain surgical mask is about 90% effective and reducing infectious droplets at 6 feet away from the patient, if worn properly.

Two standard styles of simple surgical masks that are used to reduce droplet transmission.

When should patients wear masks:

- When sitting in the waiting room in clinic-***outward protection***
- When walking on the inpatient unit (outside of their room) in the hospital-***outward protection***
- During transport to radiology or physical therapy for an exercise session-***outward protection***

When should caregivers wear masks:

- When working with patients who are on droplet precautions (for instance who have influenza infection)-***inward protection***

- When the staff member is likely to come in close contact with airway secretions (for instance a physical therapist who will be performing chest PT)-***inward protection***
- If the staff worker believes that they may have a respiratory infection-***outward protection***
- Staff members DO NOT need to routinely wear masks when entering a patient's room

FREQUENTLY ASKED QUESTIONS ABOUT MASKS

What is the proper way to use a mask?

Follow these simple instructions:

- Choose an appropriate sized mask that comfortably fits over the nose and mouth
- Perform proper hand washing prior to putting on the mask
- For "soft" masks, the colored side of the mask should face outwards
- Pinch the metallic strip on the mask so that it fits snugly on the bridge of the nose
- Adjust mask ties so that the mask fits snugly over the face
- Avoid touching the mask
- After removing the mask, discard it in a lidded rubbish bin and wash hands

Shouldn't all caregivers wear a mask when entering the room of a CF patient?

It is *not* necessary for caregivers to wear a mask when entering the room of a CF patient, unless:

- The patient has influenza infection (to protect the caregiver)
- The caregiver believes that they may have a respiratory infection (to protect the patient)
- The caregiver anticipates coming in close contact with respiratory secretions from the patient -- for instance, a physical therapist planning to do chest PT (to protect the caregiver)

Does a CF patient need to wear a mask in the physical therapy exercise room or in a clinic exam room?

It is *not* necessary for patients to wear masks during exercise in the PT room or in exam rooms, since we know that masks interfere with these treatments. There is low level air contamination that occurs with coughing during these sessions, but the air clears in less than 30 minutes (this has been carefully studied). That is why we leave these rooms empty for at least 30 minutes between patients.

Do we need to use different masks for different types of infections (different "bugs")?

For the most part, surgical masks are the best choice for CF patients for the combination of safety (the top priority), comfort and simplicity. There may be rare circumstances (such as infection with tuberculosis or similar infection), where stronger protection is recommended. The care team will provide guidance around such recommendations, if need be.

According to policy, I (a staff member) do not need to wear a mask but the patient is requesting that I wear one. What should I do?

This is a matter of sensitivity. Some patients are very worried about catching an infection during their hospital stay. While there is no evidence that having staff wear masks is of benefit to patients (other than for the reasons outlined above), it can be a reasonable accommodation to put on a mask, if it will allay patient fears. We encourage staff workers to share the information contained in this care guide with patients to promote open dialogue and education.

GOWNS AND GLOVES

There is less information about the value of wearing gowns and gloves in the hospital and clinic setting. However, there are several important reasons why it makes sense for caregivers and hospital staff to wear gowns and gloves upon entering a CF patient's room:

- It reduces the chances of clothing and equipment becoming contaminated with germs that can be carried to other CF patients' rooms
- It "slows down" staff as a reminder that handwashing should be performed (something we KNOW is very important)
- It reduces the chances of visible soiling of the hands, so that handwashing can be safely done with alcohol-based formulations (which can be more convenient to use repeatedly over the course of a typical workday)

FREQUENTLY ASKED QUESTIONS ABOUT GOWNS AND GLOVES

Do gowns and gloves really provide protection against infection?

No method of infection control is completely effective but each technique should be looked at as a tool to reduce risk. By coupling multiple techniques, like cleaning environmental surfaces, performing hand washing, wearing gowns and gloves, the risk of passing infection from one person to another can be dramatically reduced.

Should everyone entering a CF patient's room put on a gown and gloves?

Family members and friends do not need to gown and glove, since they usually have frequent contact with the patient outside of the hospital. As long as visitors will not be going to other patients' rooms, they do not need to "gown up". All hospital staff should put on a gown and gloves, even for brief visits, since we want to be consistent in how this protection is used. We know that once one person steps into a room without wearing gown and gloves, others will follow. If a patient notices a member of the hospital staff coming into the room without proper protection, it is entirely appropriate to politely ask them to "gown up".

Transmission of Respiratory Pathogens

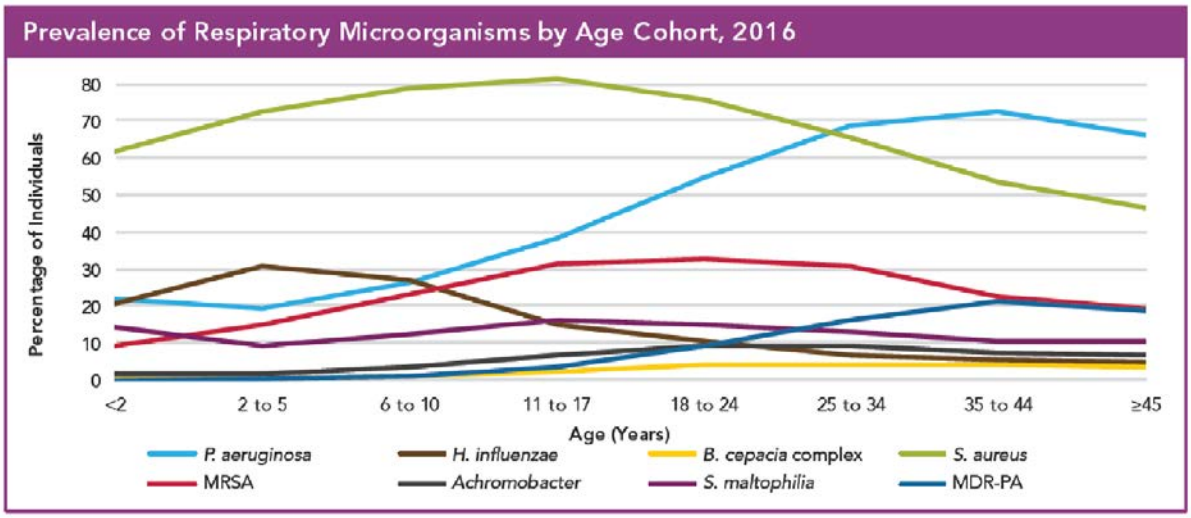
Bacteria and viruses can gain access to the lower respiratory tract by a number of mechanisms. The table below shows common modes of transmission that have been described.

Type of Transmission	Mode of Transmission	Examples of Pathogens	Sources
Contact Transmission	Direct or indirect contact with infectious secretions	• MRSA • *Pseudomonas aeruginosa* • *B. cepacia* complex • Respiratory syncytial virus	• Hands of healthcare workers • Shared toys • Contaminated respiratory therapy equipment
Droplet Transmission	Infectious droplets containing pathogens	• MRSA • *Pseudomonas aeruginosa* • *B. cepacia* complex • Influenza virus • Rhinovirus • Adenovirus • Mycoplasma • Bordetella pertussis	• Infectious droplets (generally the droplet size is >5 microns) • Droplets travel 3-6 ft • Droplets come from the respiratory tract during coughing, sneezing or chest physical therapy
Airborne Transmission	Droplet nuclei arising from desiccation of droplets containing pathogens	• Mycobacterium tuberculosis • Varicella zoster virus • Measles virus • SARS-CoV	• Airborne dissemination of droplet nuclei (1-5 microns) • Small, infectious droplets can remain suspended in the air for prolonged periods

Source: “Cystic Fibrosis Respiratory 101: Getting Started” syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Common Bacterial Pathogens

The following sections examine 3 important bacterial pathogens of the CF airway: *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Burkholderia cepacia* complex. Evidence of patient-to-patient (PTP) transmission as well as risk factors that contribute to acquisition of these pathogens are reviewed. According to the 2016 CF Patient Registry report, the prevalence of respiratory pathogens varies by age (see Figures). While the prevalence of *Burkholderia cepacia* complex carriage remains under 5%, infection with species within the complex may have profound effects on clinical outcomes and potential candidacy for lung transplantation, therefore warranting special attention.



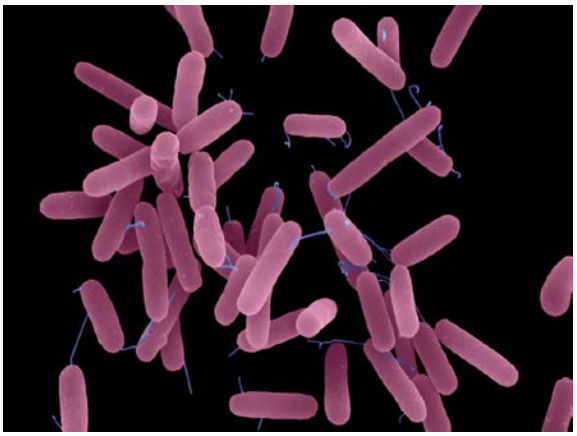
Age related prevalence of organisms in respiratory secretions of CF patients. In childhood, *S. aureus* is most common, but by the third decade this organism is supplanted by *P. aeruginosa.*

Culture Data for Individuals Seen in 2016

Bacteria	Percent with Infection	Median Age in Years at First Infection	Distinctive Features In CF
P. aeruginosa	46.4	6	• A leading cause of airway infection • Associated with a decline in lung function • 17.7% of strains are multi-drug resistant
B. cepacia complex	2.7	20	• Small proportion of people with CF infected • Can lead to rapid deterioration • Multi-drug resistant
MRSA	26.0	12	• Prevalent among people with and without CF • Multi-drug resistant • Healthcare and community-associated strains
S. maltophilia	13.1	10	• Found in water, soil, plants, animals and hospital environments • Often multi-drug resistant
Achromobacter xylosoxidans	6.3	14	• Inhabits natural environment, including soil and water • Often multi-drug resistant
Non-tuberculous mycobacteria	12.6	22	• Found in water and soil • Sporadic reports of person-to-person spread • Treatment is rigorous and often poorly tolerated

PSEUDOMONAS AERUGINOSA (PA)

PA is an aerobic gram-negative bacillus that is found in many natural habitats, including water and soil. Niches have been identified in domestic and hospital settings. Approximately 66% of adult patients who have CF in the United States harbor this organism. The process starts with acquisition, followed by attachment, leading to persistent colonization and finally chronic infection. Patients are typically asymptomatic during the acquisition phase, one of the reasons why surveillance cultures are recommended every 3 months in CF patients.



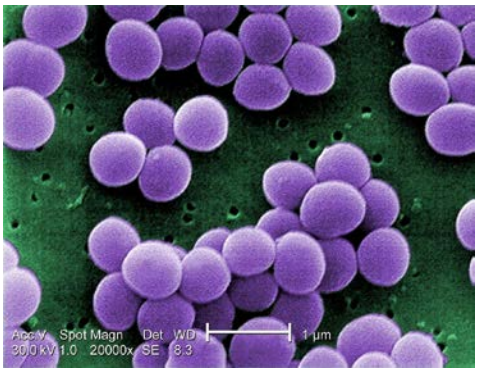
Scanning electron micrograph of *Pseudomonas aeruginosa* (pseudocolor added)
https://www.globalindoorhealthnetwork.com/gram-negative

During the attachment phase, which may be mediated by characteristics of the organism and damage to the respiratory epithelium, an initial period of intermittent colonization often precedes persistent infection. At this time most patients note a minimal change in respiratory symptoms.

Chronic infection is characterized by persistent recovery of PA from respiratory secretions for more than 6 months. During the chronic infection phase, the mucoid phenotype typically develops, which is characterized by alginate biofilm formation. Chronic infection with PA is associated with more rapid decline in lung function and shorter life expectancy. Patients with multi-drug resistant PA have even worse pulmonary outcomes. Initial colonization appears to come in most cases from environmental sources, though patient-to-patient (PTP) spread has also been documented. The prevalence of PA in CF patients seems to be declining, suggesting that strategies like early eradication and improved infection control (see sections on these topics) have had a positive influence.

STAPHYLOCOCCUS AUREUS (SA)

SA is a hardy, non-spore forming, gram-positive species that arranges itself in clusters, like grapes.

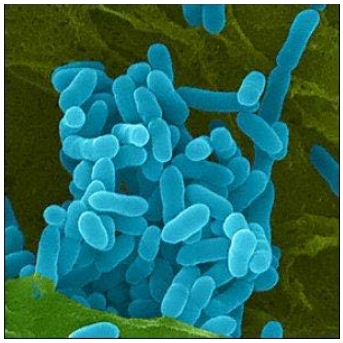


Scanning electron micrograph of Staphylococcus aureus (pseudocolor added)
https://medicalxpress.com/news/2016-06-pathogen-binding-protein-enables-rapid-isolation.html

SA frequently resides in the nasal passages or on the skin of patients with CF and in the general population. A recent study estimates the prevalence of SA nasal carriage in the general population of the United States at 32%. There is a 70% infection rate in the CF population according to the CF Patient Registry. Some isolates of SA develop resistance to beta-lactam antibiotics and carry a special designation, methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA can be found in both the hospital and community settings and the prevalence is increasing to approximately 30% of patients between ages 12 and 30. Carriage of MRSA is associated with accelerated lung function decline. Evidence of PTP transmission of SA and MRSA is well-documented, particularly in hospital settings. Repeated contact with health care facilities and use of broad spectrum antibiotics increase the risk of infection with SA and MRSA. Recent work has shown that small colony variant SA (SCV-SA), which can grow inside cells, is more challenging to treat and associated with worse clinical outcomes.

BURKHOLDERIA CEPACIA COMPLEX (BCC)

There are at least 18 designated species within the *B. cepacia* complex. Among persons with cystic fibrosis, *B. cepacia* complex is associated with five clinical syndromes: transient colonization; persistent colonization without clinical deterioration; persistent infection with clinical deterioration similar to that seen with *Pseudomonas aeruginosa* infection; persistent infection with frequent exacerbations and marked clinical deterioration; and the "cepacia" syndrome with persistently positive blood cultures and death.


Scanning electron micrograph of *Burkholeria pseudomallei* (pseudocolor added)
http://veterina.info/component/content/article/25-bolesti-goveda/185-melioidoza

A few key facts to know about *B. cepacia*:

- These organisms have innate resistance to many classes of antibiotics and have capacity to rapidly acquire new resistance through plasmid or integron exchange
- Organisms have a propensity to grow inside cells of the host. In the intracellular compartment, they are better able to escape host immune defense
- The most common species found in CF patients are *B. cenocepacia* (associated with worse prognosis) and *B. multivorans* (typically more benign course)
- One species, *B. dolosa*, is particularly virulent and highly transmissible. It has been associated with epidemic spread within a CF center and a number of deaths
- Many transplant centers will not list patients who are culture positive for *B. cepcia* complex
- Most clinical trials exclude patients who have been culture positive for *B. cepacia* complex

Species	Former genomovar designation	Habitat
B ubonensis		Human (non CF), soil
B. ambifaria	VII	Human (CF and non CF), soil
B. anthina	VIII	Human (CF), turtle, soil, plant, water, industrial contaminant
B. arboris		Human (CF), turtle, soil, water, industrial contaminant
B. cenocepacia	III	Human (CF and non CF), soil, plant, water, industrial contaminant
B. cepacia	I	Human (CF and non CF), soil, plant, water
B. contaminans		Human (CF and non CF), sheep, plant
B. diffusa		Human (CF and non CF), soil
B. delosa	VI	Human (CF), soil, plant
B. lateens		Human (CF)
B. lata		Human (CF and non CF), soil, plant, water, industrial contaminant
B. metallica		Human (CF)
B. multivorans	II	Human (CF and non CF), soil, plant, water
B. pyrrocinia	IX	Human (CF and non CF), soil, water
B. seminalis		Human (CF and non CF), soil, plant
B. stabilis	IV	Human (CF and non CF), plant, hospital contaminant
B. uronensis		Human (non CF), soil
B. vietnamiensis	V	Human (CF and non CF), soil, plant, water, industrial contaminant

Table showing different species within the *Burkholderia cepacia* complex. In CF patients the most common species isolated are *B. cenocepacia* and *B. multivorans.* http://www.antimicrobe.org/b19.asp#_ENREF_73

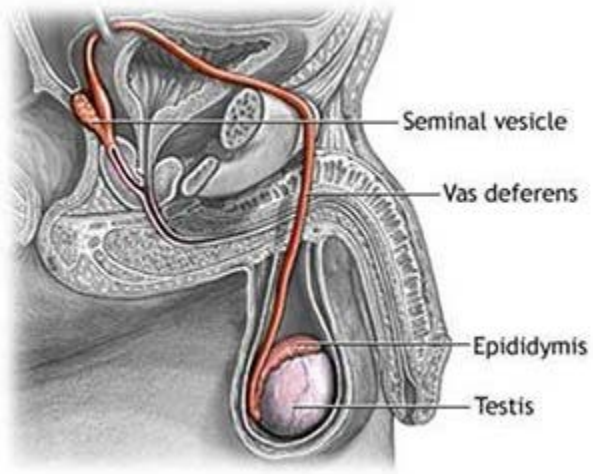
Source: "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Pregnancy and Cystic Fibrosis

Reproductive Issues in Cystic Fibrosis

Male Infertility

Most men with CF (>98%) are infertile. This can be caused by a number of different problems but is usually on the basis of congenital bilateral absence of the vas deferens,



Pain Management and Palliative Care

Before You Go Home

Hopefully, your inpatient stay has been a positive experience, helping you recover from illness, get some rest, and return home with more energy and new ideas. While you have been in the hospital, we have had a chance to get to know you better, and hopefully you have had a chance to learn more about us as well. Before discharge, it is helpful to run through a checklist yourself and with the treatment team to make discharge day go as smoothly as possible.

Several days before discharge:

- If any letters are needed for work, school or travel, let the team know (especially important are disability forms and family medical leave forms)
- Is health insurance up to date? Please speak with the team social worker if you have questions about medical coverage
- Are there labs, tests or treatments requested by outside providers that can get done while you are in hospital? Common examples include tuberculin skin testing ("TB" test), vaccinations, chest CT scans, exercise tests, sinus scans, acid reflux tests, colonoscopy.
- Do you need any new equipment prior to going home or will equipment need to be serviced/repaired?

The day before discharge:

- Meet with discharge planner and possibly with a home care company (if you will have home IV therapy, supplemental oxygen and/or a breathing device)
- Do you need refills for any medications from home?
- Will you be on any new medications after leaving the hospital?
- Are there special instructions to go with new prescriptions?
- Do you have a hospital follow up appointment with the team (should be scheduled 2-3 weeks post discharge)?
- Have you organized all of your personal items and packed those things that will not be needed prior to return home?
- Confirm your arrangements for transportation--leaving before noon allows other patients to be admitted earlier in the day

The day of discharge:

- Confirm that all prescriptions are up to date
- Pick up new prescriptions or refills that have been placed at the Maine Medical Center Pharmacy
- Confirm the time and date of follow up appointment
- Review your discharge paperwork with your team carefully and clarify any questions you may have

Resources for Your Hospital Room

The hospital can provide a number of important things to you--sometimes you simply need to put in a request to your treatment team.

- **Room refrigerator**--This should be in your room on arrival.
- **Television**--Every room is equipped with a television.
- **Fan**
- **Humidifier**
- **Air conditioner**
- **Laptop computer**--Wireless internet access is available using network name "mhguest". Please be aware that your internet activity may be monitored and certain websites may not be appropriate for hospital viewing
- **Flat screen TV with DVD player** (a wide selection of movies is also available)
- **Wii Fit for use in the room**. Please ask physical therapy about this activity.
- **Manipulative therapy**--Helps with range of motion, relaxation, and relief of pain
- **Massage therapy**-- Three nurse massage therapists are available to inpatients. Patients must pay at the time of service. With a physician's order, patients can submit charges to their insurance company for reimbursement.
- **Reiki Program**-- A Japanese technique to reduce stress and promote relaxation, Reiki is a gentle laying on of hands or holding the hands just above the body, which allows energy to flow through the hands of the Reiki practitioner into the body of the receiver. Our Reiki practitioners are trained, certified, and caring volunteers who will come to your room to provide your session. You, a healthcare provider, or a family member may call the Reiki line at 207-662-4473 to request a Reiki session
- **Spiritual care consultation**--Feel free to talk to your nurse or treatment team, if a spiritual care visit is of interest to you. We will arrange having a member of the spiritual care team come to your room.

Sample Daily Schedule

Your inpatient admission is a time to get all of your needed medications and therapies. We encourage all patients to maintain a healthy sleep schedule, as medications and therapies have to be delivered during morning hours. Below is a typical daily schedule, though this schedule will be individualized for each patient. This schedule does not include time spent with the nursing assistant, phlebotomist or nurse for daily measurements, lab studies and IV antibiotic treatments.

0700	Wake up/shower
0830	Pre-breakfast medications
	Breakfast
0900	Inhaled medications
0930	Physical therapy/Airway Clearance
1000	Medical team rounds
1200	Pre-lunch medications
	Lunch
1300	Free time/Exercise Room/Daily Walk
1500	Physical therapy/Airway Clearance-Exercise
1600	Free time/Exercise Room/Daily Walk
1800	Pre-dinner medications
	Dinner
1900	Free time
2000	Vest use/Airway Clearance
2030	Free time
2200	Bedtime

The Inpatient Team

This section is written for patients who are hospitalized and serves as an introduction to the many people who are on the care team and the roles that they play. It may seem a bit overwhelming to have so many people involved in the care plan during a hospital stay, but each person brings something important to treatment.

Med-Surg Nurses-practice primarily on hospital units and care for adult patients who are acutely ill with a wide variety of medical issues. They provide care 24/7 and have more facetime with patients than any other professional in the hospital. They deliver regularly assess patients, deliver medications, provide education, and help prepare the patient and family for discharge from the hospital.

Nursing Assistants-play a supportive role to nurses by checking vital signs and blood sugars. They may also help patients with activities of daily living (if necessary) like mobility, bathing, dressing and eating.

Primary Physicians-are board certified physicians who specialize in hospital care. They oversee the day-to-day plan of inpatient care in tandem with the CF specialists. They are also in charge of the decision to discharge patients from the hospital.

Physician Assistants-are highly trained and skilled medical practitioners who work under the supervision of a licensed physician. They are available to see you 24/7 and can order tests and treatments.

Medical Students-are *college graduates* who are studying to be doctors in medical school. Medical students play an important role on the treatment team by gathering information for team rounds (lab and x-ray results, outside records, etc.). Some medical students may go on to become future CF specialists, so their interaction with you may be important in helping them reach that decision.

Medical Residents-are *licensed physicians who have graduated from medical school*. Residents also play an important role on the treatment team by gathering information for team rounds and by placing orders for tests and treatments. Some residents may go on to become future CF specialists, so their interaction with you may be important in helping them reach that decision.

Fellows-are *licensed physicians who have completed residency training and are now specializing in a particular area of medicine* (usually lung medicine, if they are involved in your care). Some fellows may go on to become CF specialists after completing fellowship, so their interaction with you may be very important in helping them reach that decision.

Consultants-are specialists who help the primary team answer specific, more complex medical questions and also assist with treatment decisions in those situations. Examples of situations where consultation

may be requested include sinusitis that may require surgery, gastrointestinal disorders, post-transplant medication adjustment, or kidney problems.

Physical Therapists- treat patients by teaching them different exercises intended to strengthen or stretch muscles as well as alleviate pain and improve movement. Physical therapists also help with airway clearance, finding the best method for each patient, which may include chest PT or other techniques.

Respiratory Therapists-help patients who have trouble breathing. They provide aerosol and oxygen treatments, perform breathing tests, and set up ventilatory assistance equipment like CPAP or BiPAP (explained in other sections). They may also assist with certain types of airway clearance.

Manipulative Medicine Specialists (Neuromuscular Medicine)-perform osteopathic manipulative treatment, or OMT, is hands-on care. It involves using the hands to diagnose, treat, and prevent illness or injury. OMT involves moving muscles and joints using techniques including stretching, gentle pressure and resistance.

Dietitians- are trained to provide advice and counselling about diet, food and nutrition. They help people make healthy food choices, separating fact from fiction and distinguishing healthy eating plans from those that don't provide optimal nourishment. They also make recommendations about tube feeding formulations and vitamin replacement.

Social Workers- help people solve and cope with problems in their everyday lives and help them get the resources they need. Some social workers also diagnose and treat mental, behavioral, and emotional issues.

Spiritual Care Specialists- serve to help address what we call the "big" questions of life. These questions can include:

- Why is this happening? Why is it happening to me?
- What does it all mean?
- How do I make sense of everything?
- What gives me comfort and hope?
- What do I call "good" in my life? What do I call "bad"?
- What am I grateful for?
- What do I trust? Who do I trust?
- Who is my "beloved community" -- who loves me and is loved by me, no matter what?
- What or who -- beyond myself -- do I believe is important in my life?

Some people find meaning, comfort, hope, goodness and community through their religious practice, beliefs and/or community of faith. Some people do not. Regardless of whether religious faith is a part of a person's life, spiritual concerns, resources and needs can still be very important, especially during hospitalization.

Discharge Coordinators- make sure that patients leaving the hospital be able to continue their recovery from home or wherever they are going. They team up with social workers and home care teams to firm up plans for home IV therapy, tube feedings, new equipment and post-hospital care.

Suggested Packing List for the Hospital

- **Specialty Medications** (not on the inpatient hospital formulary). Common examples would be ivacaftor (Kalydeco®) or ivacaftor/lumacaftor (Orkambi®)
- **Therapy Vest and/or Home Percussor** (at least try to bring the Vest, even if you cannot bring the compressor unit)
- **BiPAP/CPAP/or AVAPS machine and mask**
- **Laptop computer, tablet and phone**--with charging cables
- **Books** or other reading materials
- **Clothes**
- **Pajamas**
- **Workout clothes**--for example, sneakers and shorts/t-shirt
- **Bedding and pillows** (the hospital will provide these, but bedding from home may help with better sleep)
- **Toiletries**
- **Snacks**

Welcome to Inpatient Care

You will be seen by a wide variety of practitioners during your stay. This includes hospitalists (physicians and advanced practice professionals (APP) trained in hospital medicine), pulmonary and CF specialists, physicians-in-training, nurses, nursing assistants, respiratory therapists, physical therapists, nutritionists, social workers, phlebotomists (who draw blood), radiology technicians, and other staff. All of these various people you will meet during your admission work as a team and do their best to communicate with one another. However, because you will be in contact with a large number of different people during the hospital stay, and because this is a teaching institution, you may find some of them not as familiar with cystic fibrosis as your primary CF team. Your willingness to teach your team members about how you usually treat your CF and how it affects YOU is really appreciated by us.

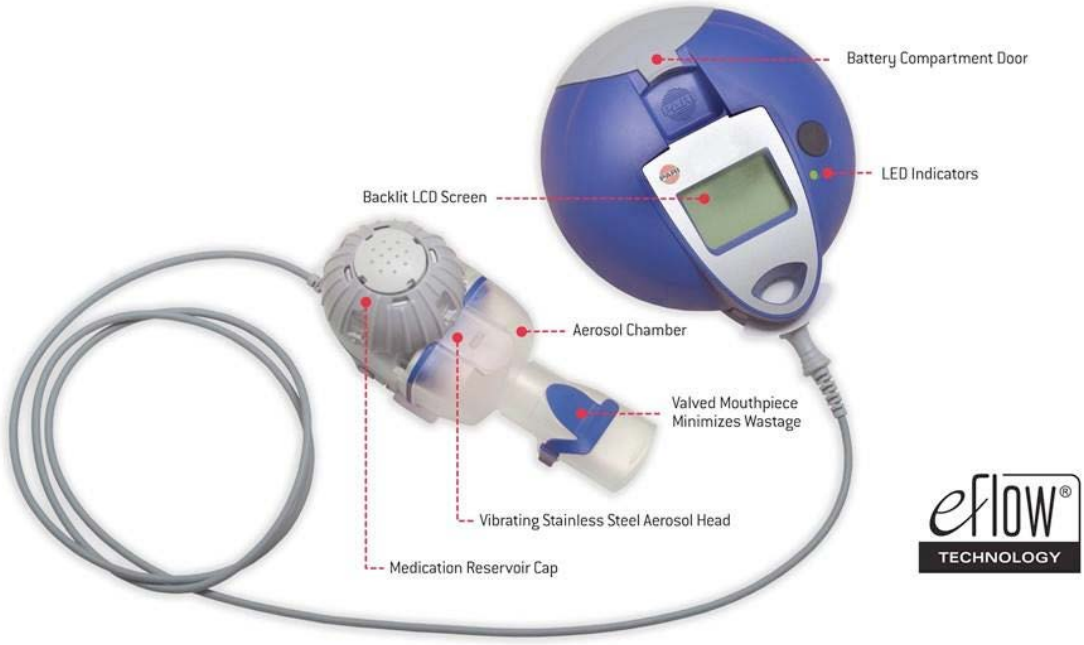
Your CF specialists (Drs. Zuckerman and Sears) will help set the overall goals of care with you and communicate this to the inpatient team. They will visit you regularly but not necessarily every day during the hospitalization. On a day-to-day basis, the hospitalist team (hospitalist physician and APPs) will be in charge of adjusting the plan and dealing with new issues that may arise. Your nurse, respiratory therapist, physical therapist and nutritionist will work together with your doctors to fine tune the plan in their area of specialty and deliver the care that you need.

Your admission is a time to focus on your recovery from illness. That includes scheduled delivery of medications and treatments that will help you feel better as quickly as possible. This time is also important for getting rest, nourishing yourself with healthy food and putting aside some space in your day to direct your thoughts and activities in a positive direction. Your team will encourage and remind you about the schedule and your therapies, but your active participation in your care is the most important thing that will help you recover as quickly and completely as possible.

eFlow®Nebulizers: Use and Care

The PARI eFlow® electronic nebulizer is a new-generation aerosol delivery platform that incorporates technologic advances that significantly improve inhaled medication delivery. The aerosol generator (or aerosol head) of the eFlow® platform consists of a vibrating, porous, stainless steel membrane with thousands of tiny laser-drilled holes. It is small, quiet, portable, and operates with batteries or AC current. It produces aerosol faster and is more efficient than jet nebulizers, making it very attractive for use with CF drugs. The aerosol head operates by vibrating rapidly next to the liquid drug, thus pumping the liquid through the tiny holes to create the aerosol for inhalation.

The eFlow® is also more efficient at delivering drug to the lungs because it doesn't waste as much as jet nebulizers. There is almost no drug left in the chamber at the end of nebulization, and the aerosol chamber conserves nebulized drug during patient exhalation, making more drug available for the next inhalation. For a brief demonstration of how the eFlow® works, see the video on the PARI website at http://www.paripharma.com/technologies1.htm

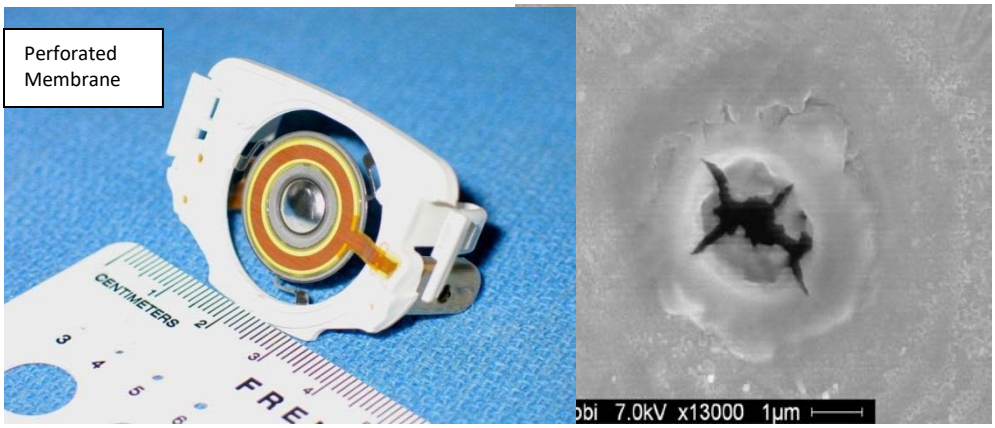


The eFlow® consists of an electronic "controller unit" (right) and a "handset" (left). The aerosol head is mounted inside the handset and operates without noise.

There are two commercial types of the eFlow® in the U.S. The Trio® (formerly the eFlow® SCF) is available from a limited number of specialty pharmacies that provide CF drugs to patients, and compound drugs for use with the Trio. The Altera® is the name for the eFlow® customized for use with Cayston® (aztreonam lysine for inhalation), a recently approved inhaled antibiotic. The Trio and Altera have very similar configurations and function. With the approval of Cayston® , these eFlow® devices will be more widely available to CF patients. Though the labeling for the Altera nebulizer states that it is only to be used for Cayston® , we expect there will be a desire to use it for other CF medications to reduce the delivery time. Since these other drugs have not been adequately clinically tested with eFlow®, it is *crucial* to understand the benefits and the risks of off-label use of these drugs, and how to properly use, clean and maintain the

device.

The first prescription of Cayston® comes with the Altera nebulizer, one controller unit and two handsets. Thereafter, each refill will come with a new handset. Cayston® approved for use 3 times a day, and each dose takes about 2 minutes to nebulize. If handled properly, the aerosol head can last for 3-6 months or longer, depending on how many times it is used. That means that after a cycle of Cayston® , the aerosol handset should still operate effectively for several more weeks. The main reason that the handset stops working is that the tiny holes in the membrane get clogged over time, so it takes longer to nebulize a dose. To prevent this, it is very important to clean the handset *immediately* after each use. It is also recommended that the handsets be disinfected after each use.



The metal membrane in the center of the nebulizing head has thousands of microscopic holes that cannot be seen with the naked eye (left). The holes can become clogged over time (right; magnified x 13,000)

USING THE ALTERA® OR TRIO® WITH CF DRUGS

The eFlow® devices were designed to be used with specific drugs. It is important to recognize that there are no clinical trials to validate the effectiveness or safety of other CF drugs with eFlow® nebulizers. The information about the use of eFlow® with other drugs comes mostly from bench aerosol studies, small scintigraphy and pharmacokinetic (PK) studies, and anecdotal experience. These studies show that the predicted lung dose using the eFlow® is about twice that of the PARI LC PLUS™, and about 4 times that of less efficient t-piece nebulizers (1-3). Because of the large treatment burden in CF, there is a natural temptation to use the eFlow® with other drugs (off-label) to reduce that burden. *Please note that the following information is not a recommendation to use off-label drugs with eFlow® devices*; rather it is a guide for those who choose to do so. The goal of this document is to provide guidance on the safe use of the eFlow® based on available information and to minimize potential toxicity due to high drug exposures.

- **TOBI®** comes in ampules containing 300 mg in 5 mL of fluid. The PARI LC PLUS jet nebulizer combined with the DeVilbiss® Pulmo-Aide® compressor is the approved delivery system for this drug. Aerosol device studies and small PK studies show that about half the dose of tobramycin in the eFlow® would approximate the lung dose of TOBI® delivered by the LC PLUS (1, 4-5).
- **Colymycin (colistin)** comes in 150 mg vials, and is mixed with water or saline to nebulize. The CF Pulmonary Clinical Practice Guideline "Chronic Medications for Maintenance of Lung Health" states that there was insufficient evidence to recommend the use of colistin (6). Since colistin is not approved by the FDA for inhalation, there is no gold standard for delivery. The eFlow® is 2 to 3 times more efficient than most jet nebulizers used for colistin. Commonly between 75 mg (1/2 vial) to 150 mg (full vial) of colistin is used in jet nebulizers. With the eFlow®, it is estimated that between 50 to 75 mg (1/3 to 1/2 vial) would achieve similar levels of colistin in the lungs (7,8).
- **Hypertonic saline** is commercially available as Hypersal™ 7% in 4 mL ampules, or is prepared by pharmacies in varying concentrations. Since the eFlow® leaves almost no residual (unlike jet nebulizers),

2.5 to 3 mL should approximate a routine nebulizer dose.

- **Bronchodilators -** Inhaled beta2-agonists and anticholinergic agents are not without side effects, so a doubling or quadrupling of drug delivery to the patient may actually increase toxicity risk without an increase in benefit (dose-response curve plateaus at low doses). If the eFlow® were used for bronchodilators, a significant reduction in nominal dose may be necessary to avoid toxicity. These drugs have side effects including fast heartbeat, muscle tremors, and nervousness. With the efficient eFlow®, it is *very important* to reduce the dose of these drugs by *at least half* to avoid toxicity. If side effects still occur, lower the dose again, or consider alternate delivery systems (2).
- **Dornase alfa** (ampules of 2.5 mL =2.5 mg) can be delivered with a number of approved nebulizers. The eFlow® does not damage the protein drug during nebulization (9). While the eFlow® can deliver 2-4 times as much as the approved nebulizers (3), this drug is very safe, so there is minimal concern about increased side effects with a higher dose. It is possible that the higher lung dose will allow some people who take dornase alfa twice a day to reduce the frequency to once daily and still retain the benefit, though this would have to be tested clinically in each individual.
- **Budesonide in Respules** is an inhaled steroid suspension, with tiny particles of drug suspended in fluid. The pulmonary clinical practice guideline "Chronic Medications for Maintenance of Lung Health" recommends against the routine use of inhaled corticosteroids in CF unless there is co-existing asthma (6). Since the particles of drug can plug up the holes in the eFlow® membrane, one should not use this drug with this device.

Drug	Usual Jet Nebulizer Dose	Suggested eFlow® Dose
TOBI®	**300 mg**	**150 mg**
Colistin	**75 - 150 mg**	**50 - 75mg**
Hypertonic Saline	**4 mL**	**2.5 - 3 mL**
Bronchodilators	**1 ampule**	**½ ampule**
Dornase alfa	**1 ampule**	**1 ampule**
Budesonide Respules	**1 ampule**	**Do not use**

CLEANING AND DISINFECTING eFLOW® DEVICES

Instructions for cleaning and disinfection come with the devices, so the emphasis here will be on how to maintain the function of the aerosol heads for as long as possible.

- **Immediately after each use, disassemble the handset and wash the pieces as directed**. If there is not enough time to wash in soapy water and rinse, then at a minimum rinse the parts with tap water and let it run through the aerosol head for at least 10-15 seconds. If this is not done each time, there is a risk that dried drug residue will block the membrane and cause it to malfunction. After washing, either place the parts in the sterilizer or let the parts air dry completely on a clean towel between uses.
- If using more than one drug with a single handset, rinse well between drugs to avoid drug

interactions in the reservoir.

- **Never touch, scrub, or brush the metal aerosol head**. It is easily dented or scratched, which will cause it to malfunction.
- Many techniques for disinfection *should not be used* with the eFlow® devices, including bleach, hydrogen peroxide, alcohol, and boiling. The Altera® instructions recommend disinfectants like Control 3, but an electronic steam sterilizer like those used for baby bottles (e.g., Nuk Quick 'n Ready) may also be used. Do not use the type of sterilizers that are placed in the microwave. Steam sterilizers not only disinfect the devices quickly, but they also help to maintain the life of the aerosol head.

Baby bottle steam sterilizers can be used for eFlow® handsets and jet nebulizers.

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Equipment Use and Care

- Use of high speed nebulizers
- Care of nebulizers
- Vest use

Care of Nebulizers

- Clean non-critical items with a detergent. *Category II*
- Manage all respiratory therapy equipment, e.g., handheld nebulizers and tracheostomy tubes used in the home setting according to the same principles applied in the hospital setting. *Category IB*
- Clean thoroughly by removing all respiratory tract secretions from reusable objects that touch mucus membranes by washing with soap and water as soon as possible after each use. Dried, caked materials should be thoroughly cleaned from surfaces because disinfection is impaired by films or crusts of organic substances. *Category II*
- **DO NOT** use vinegar, bleach, or Control III (benzalkonium chloride) solutions to disinfect reusable respiratory equipment that touches mucous membranes**.** *Category IB*
- Disinfect these reusable items, <u>if acceptable according to the manufacturer's recommendations,</u> with one of the following methods:

  1. Clean nebulizer parts with dish detergent soap and tap water.
  2. Disinfect using one of the following methods:
     - Boil in water for five minutes. *Category IB*
     - Microwave (submerged in water) for five minutes. *Category IB*
     - Use a dishwasher, if the water temperature is 158 degrees or higher and maintained for at least 30 minutes. *Category IB*
     - Use an electric steam sterilizer
     - Immerse* in one of the following:
       . 70 to 90% ethyl or isopropyl alcohol for five minutes.
       . 3% hydrogen peroxide for thirty minutes.

     *If immersed in alcohol or hydrogen peroxide solution, rinse with sterile water or filtered water (0.2 micron pore size), not tap, bottled, or distilled water. *Category II*
  3. Finally, air-dry all equipment before storage

<u>Category Key:</u>

Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

Category IC. Required for implementation, as mandated by federal and/or state regulation or standard.

Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

No recommendation; unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exist.

Not applicable. Limited evidence was found by the systematic review conducted for the 2013 IP&C guideline; thus, the grading of evidence was not used.

% Agreement Consensus. <u>≥</u> 80% agreed with statement by anonymous voting

Certainty: low. < 80% agreed with statement by anonymous voting and thus insufficient evidence exists to recommend for or against

Adapted from "Cystic Fibrosis Respiratory 101: Getting Started" syllabus by Richards, K, Seidelman, J, Lester M. 2015, Cystic Fibrosis Foundation online resource.

Frequently Asked Questions

1. ***Can I get a "day pass" to leave the hospital?*** Unfortunately, for legal reasons, the hospital is unable to let patients have "day passes" or temporarily leave the hospital grounds.

2. ***Where am I allowed to walk in the hospital?*** You are allowed to visit the cafeteria, the interior (outdoor) atrium near the cafeteria, along with gift shop and cafe. You may also walk around your floor or unit. With accompaniment you may be able to walk around the outside of the hospital grounds, weather permitting. Please note that you must follow infection control recommendations when outside your room, including wearing a mask and gloves and potentially a gown.

3. ***Why do I have to wear a mask/gown/gloves?*** There are many patients, perhaps even on the same floor that you are staying on, that have weakened immune systems. Bacteria that CF patients carry, including *Staphylococcus aureus* ("Staph") and *Pseudomonas aeruginosa* ("Pseudomonas"), can be transmitted to other patients and cause life-threatening infections.

4. ***How long do I need to stay in the hospital?*** *Why are some CF patients discharged sooner (or later) than others?* Each person is different, and your care team attempts to individualize your care to come up with the best plan for you. While we usually plan for two week courses of IV antibiotics, this may be shortened or lengthened depending on the specific situations. Similarly, while we are sometimes able to discharge patients on home IV antibiotics after shorter hospital stays, at other times longer stays in the hospital are medically necessary. Drs. Zuckerman and Sears will discuss your individual plan with you.

5. ***Can I request a specific room or floor?*** We are happy to pass along requests to the admissions office, although many factors, including the number of other admitted CF patients, the number of available nurses, and overall hospital bed occupancy may determine whether it is possible to be assigned a given room or floor. In many instances we may unfortunately not be able to successfully accommodate specific requests for rooms.

6. ***May I use medical marijuana?*** Medical marijuana is not allowed by hospital policy (based on federal law). Symptoms that are treated with medical marijuana can often be treated with other medications as well; please discuss this with your treatment team.

7. ***Why can't I use my medications from home?*** For safety reasons, the hospital has a policy to have medications dispensed by the hospital pharmacy to the inpatient units. In this way each medication can be checked for appropriate dosing and for potential interactions with other medications. In certain circumstances where a medication is not on formulary in the hospital pharmacy, you may be asked to bring your medications with you to the hospital. In general these "non-formulary" medications will still be stored for you in a manner that allows the pharmacy to cross check the medications against your other prescribed treatments.

8. ***Can I have all of my blood work drawn through my port or PICC?*** Studies have shown that using central venous catheters for routine blood draws raises the risk of catheter and/or blood stream infection. In addition, blood draws increase the risk for blood clots to form in the catheter. Therefore, MMC has a policy of not using these catheters routinely for blood draws. However, when the port is first accessed or when the PICC is placed blood may be withdrawn for laboratory studies as part of the flushing protocol. Please speak with your care team if you have concerns or questions about your particular situation. We want to work with you to provide the safest and most comfortable care possible during your hospital stay.

Pulmonary Exacerbation FAQ for Providers

1) Why are we admitting these patients (they don't look that sick)?

Cystic Fibrosis is a genetic multisystem disease, causing significant damage and disruption to multiple organ systems; however, most CF patients die of respiratory complications of progressive lung disease.

Exacerbations, defined broadly as episodes of increased cough, sputum, and dyspnea, are typically associated with acute decline in lung function. Effective treatment of an exacerbation can reverse such decline in lung function, whereas failure to treat may lead to permanent damage. In fact, even with in hospital treatment approximately 25% of patients do not return to previous baseline lung function 3 months following treatment. So, while it is true that very few CF patients are in danger of death over the short term from an acute exacerbation (especially when they have good baseline lung function), over the longer term, admitting these patients has become an accepted part of aggressive, proactive care. Please know that prior to admission many patients have received 1-2 weeks of augmented outpatient therapy without returning to baseline.

Admitting these patients when they have an exacerbation serves a number of purposes. First, it allows us to provide therapy in an environment where we can be sure the patients are getting it as prescribed. Second, it allows us to monitor lung function closely in a controlled environment. Third, it facilitates addressing other issues that frequently complicate pulmonary exacerbations (such as, volume depletion, malnutrition, sinusitis, exhaustion, chest pain, hemoptysis, and poorly controlled diabetes).

2) What are the important treatment components for a pulmonary exacerbation?

Treatment of an exacerbation primarily focuses on three medical components; IV antibiotics, airway clearance, and supportive care. At Maine Medical Center (MMC) we also emphasize supervised exercise as an important adjunct to standard care. The decision to schedule admission is made jointly by the patient and care team when it seems that treatment will be better achieved in the hospital environment than at home. Increasingly, insurance play active role in the process, by pre-approving admissions and monitoring the inpatient record to confirm that hospital-based treatments are consistently transpiring. Thus, in those cases where a patient is unable (or unwilling) to accept prescrbed therapies, it is important to discuss with the CF care team whether inpatient treatment is necessary.

3) What are the components of airway clearance (a term preferred by patients and staff over "pulmonary toilet") for admitted CF patients?

The mainstay of airway clearance is chest physiotherapy (CPT) provided by a physical therapist (PT). It is imperative that **every admitted CF patient meet at least twice daily with PT**. Ideally, patients should get 30 minutes of manual CPT twice daily, along with wearing a high frequency oscillator vest (the "Vest") or receiving treatment with a hand-held percussor-vibrator for at least 30 minutes 2-3 times per day. At MMC exercise is used as an important adjunctive airway clearance measure. While it should not be viewed as a stand alone airway clearance modality, in practical terms PT typically replaces the afternoon CPT session with supervised exercise in those patients who are able. Certain medications

greatly facilitate airway clearance. These include inhaled dornase alpha(Pulmozyme™, which is recombinant human DNase) for most patients, and for some, use of 3% or 7% hypertonic saline (Hyper-sal) and bronchodilators. (See Airway Clearance flow diagram).

It is critically important that airway clearance not be overlooked in post-op patients or in those experiencing chest or abdominal pain. IF AIRWAY CLEARANCE CANNOT BE ACHEIVED AS SCHEDULED ON THE REGULAR MEDICAL UNIT, THIS MAY BE AN INDICATION FOR A HIGHER LEVEL OF CARE. Inability to provide regular airway clearance for any reason should prompt communication with the pulmonary consult team and/or CF specialist.

4) How do we know what IV antibiotics to use for a patient?

This is a complex question that is under active investigation in clinical trials. Interestingly, in CF *in vitro* ANTIBIOTIC SUSCEPTIBILITIES ON SPUTUM CULTURES DO NOT ALWAYS PREDICT CLINICAL OUTCOMES. Thus, while we do review susceptibilities, there are multiple other factors that come into play when finalizing antibiotic selection, such as the patient's tolerance of certain drug classes, response to prior regimens, and comorbidities. In some cases, such as when a patient harbors several multi-drug resistant organisms there may not appear to be an optimal regimen. That being said, for patients harboring *Pseudomonas aeruginosa*, it is standard practice to use two drugs that treat through different mechanisms of action (i.e., a cell wall agent and aminoglycoside, or a cell wall agent and quinolone). Once a regimen has been selected, maintain it and change it only if there is “clinical failure” (as opposed to a culture which shows resistance). At MMC several biomarkers are used to assess response to treatment:

- WBC
- CRP
- Weight
- FEV1
- Oxygen requirement

Baseline values are generally rechecked after one week of therapy to determine adequacy of response. Feel free to discuss the measurements with the CF specialist.

5) Do CF patients require different antibiotic dosing?

It is often not recogized that the pharmacokinetics and pharmacodynamics of many drugs are altered in CF patients. Nowhere is this more important than in antibiotic dosing, where the treatment target (bacteria trapped in airway biofilms) is not easily reached by the circulation. Many beta lactam antibiotics exhibit increased serum protein binding (thus increasing the volume of distribution) and more rapid clearance from serum. Since these agents provide time-dependent killing, it is important to try to keep serum concentrations above the minimal inhibitory concentration (MIC). A commonly employed strategy is to use high doses of medication delivered through prolonged infusions (from 3-24 hours). The slow infusion formulations used at MMC can be easily found in the Epic CF orderset. Quinolones tend to be more rapidly cleared from CF patients, so more frequent dosing is recommended.

For example, ciprofloxacin should be infused every 8 hours rather than every 12 hours. Oral formulations should generally be avoided in the hospital due to unreliable absorption in CF patients and the desire to achieve high tissue levels during exacerbations. Aminoglycisides exhibit concentration-dependent killing, where it is important to achieve a high peak concentration of drug. There is a post-antibiotic effect with these medications, so it is NOT important to keep the serum level above MIC (in fact it is very important to maintain a low trough level to avoid nephro- and ototoxicity). At MMC we use once daily aminoglycoside dosing at 10-12 mg/kg/day and the first dose should be at 9 am so that trough levels can be easily checked in the hospital and outpatient settings. We are fortunate to have an excellent ID pharmacy team. Please avail yourselves of their expertise.

6) How long do we treat patients with IV antibiotics?

Standard care is to treat for 2 weeks with IV therapy, though a large multi center trial is currently addressing this important question. In rare situations we may opt for a shorter course (or change to oral antibiotics). More frequently (especially in patients with advanced disease), we will use more prolonged courses for up to 3-4 weeks. However, for many patients IV therapy can be completed at home once it is clear that they are improving. It is important in these instances to know that adequate support is in place (insurance coverage and means for airway clearance) to complete treatment in the home setting. We do not transfer patients rehab centers, skilled facilities or nursing homes to complete IV antibiotics. Our team social worker and CF specialist can help to navigate these issues.

7) Do CF patients need systemic steroids for exacerbation?

We typically do not use systemic steroids for exacerbations. Hyperglycemia and premature osteoporosis are common in CF adults and can be worsened by repeated steroid challenges. A subset of patients patients have reactive irways disease and find inhaled bronchodilators and steroids helpful. For those patients, brief courses of oral steroids during treatment of exacerbations are often useful-- on the order of 10-20 mg prednisone equivalent daily. Some patients, especially those with asthma, allergic bronchopulmonary aspergillosis (fairly common in the CF population), or post-solid organ transplant will also end up on chronic low dose steroids and may require increases during exacerbations. Selected patients with end stage lung disease, sinusitis, arthritis or allergies may also benefit from systemic steroids. Description of long term steroid use is found in the outpatient record and should be discussed on a case by case basis with the CF team.

8) How is CF related diabetes (CFRD) different from other diabetes?

CFRD is a unique form of diabetes caused by progressive destruction of the endocrine pancreas. Nearly 50% of CF adult develop abnormal glucose tolerance. CFRD is treated somewhat differently than either Type I (autoimmune) diabetes or Type II (insulin resistant) diabetes. Like Type I diabetes, there is loss of insulin production in CFRD, and medical therapy is restricted to the use of insulin. Similar to type II diabetes, ketoacidosis rarely occurs, as CFRD is characterized by residual, albeit inadequate, endogenous insulin production. Thus, it is extremely rare to need an insulin drip or even an aggressive sliding scale. To complicate matters, many patients also suffer from delayed and suboptimal counterregulatory glucagon secretion and are at increased risk for symptomatic hypoglycemia, particularly if food intake is diminished. Therefore, use of sliding scales at MMC is generally discouraged in this patient population.

Many times patients use long acting insulin, and we will eventually add meal coverage. When fasting, some patients will not require insulin at all, while others will require a reduced dose of long acting insulin. Long acting insulin may be administered in the morning in some cases rather than at night, if morning hypoglycemia is a recurring problem. Other patients require an insulin pump to approximate normoglycemia.

There is some evidence that early institution of insulin herapy may mitigate premature lung function decline, so you may find some patients on low doses of insulin in patient despite exhibiting only mild post prandial hyperglycemia.

Finally, it bears repeating that **CF patients require a high fat, high calorie diet and should not be put on a diabetic diet.** Better to use glucose readings to provide education about avoiding concentrated sweets (such as candy and soda) and adjust the insulin regimen for the following day. Formal input from endocrinology can be very helpful in problematic cases.

9) What are the key points to know about infection control in CF patients?

This is an important issue that leads to considerable confusion among patients, family and medical staff. All CF patients should be treated with contact precautions. All staff should ALWAYS don precaution gowns and gloves upon entry to patient rooms along with performing appropriate hand hygiene. We are trying to minimize transfer of respiratory pathogens between CF patients, as has been documented at multiple hospitals prior to the institution of stricter infection control policies. Each patient room should also have a box of standard surgical masks in the door caddy. The need for masks is controversial. At MMC masks are provided for staff members who may come in close contact with respiratory secretions (for instance, physical therapists who will perform CPT). Staff members are also encouraged to wear a mask if they have a respiratory infection in order to minimize patient exposure. Occasionally, patients may request that a provider wear a mask, particularly if the patient is post-solid organ transplant. We encourage providers to respect this request, understanding that this is not an evidence based practice. Otherwise, masks do NOT need to be worn. Each unit should have a copy of the institutional infection control policy for CF patients. Detailed information will also be available electronically in the Adult CF Resource manual.

Patient Rights & Responsibilities

PATIENT RIGHTS

All patients (and when acting on behalf of a patient, a patient representative) have the following rights:

- To receive safe, considerate and respectful care
- To have his or her cultural, psychosocial, spiritual, and personal values, beliefs and preferences respected
- Personal dignity
- To have their confidentiality, privacy and security respected
- To have access to an environment that preserves dignity and contributes to a positive self image
- To be free from mental, physical, sexual and verbal abuse and exploitation
- To be free from restraints that are not medically necessary and to be free from seclusion or restraint that is imposed as a means of coercion, discipline, convenience or retaliation
- To pain management
- To access protective and advocacy services
- To be informed about the care they will receive in a manner and/or language that he or she can understand
- To have pastoral and other spiritual care services accommodated within the limits of the law and Maine Medical Center's capabilities
- To consent to or refuse a treatment, as permitted by law
- Designate visitors of his or her choosing, unless no visitors are allowed (including designated hours of visitation) or it is reasonably determined that the presence of a visitor or visitors would endanger the health and safety of a patient, a staff member, or would significantly disrupt the operations of the facility
- To receive adequate information in order to consent to or decline to take part in research studies and to know that refusal to take part in research (or discontinuing participation) will not compromise his or her access to care, treatment and services not related to research

PATIENT RESPONSIBILITIES

- Providing information: Patients and families, as appropriate, must provide to the best of their knowledge, accurate and complete information about present complaints, past illnesses, hospitalization, medications, and other matters relating to the patient's health. Patients and families must report perceived risks in their care and unexpected changes in their condition by providing feedback about service needs and expectations

- Asking questions: Asking questions when they do not understand their care, treatment and service or what they are expected to do
- Following instructions: Patients and their families must follow the treatment and service care plan that is developed for the hospital stay. They should express any concerns about the ability to follow the proposed plan and every effort should be made to adapt the plan to the specific needs and limitations of the patient. When these adaptations are not recommended, patients or families should be informed of the consequences of the alternatives and of not following the proposed course, including their responsibility for outcomes related to not following the care, treatment and service plan
- Following Maine Medical Center's Rules and Regulations
- Showing respect and consideration, including to Maine Medical Center staff and property, as well as other patients and their property

Abridged from MMC Policy: Patient Rights and Responsibilities 11.2010

Standard Precautions Policy

MAINE MEDICAL CENTER
INSTITUTIONAL POLICY MANUAL

Policy Title: Standard Precautions

Summary:
Standard Precautions combines the major features of Universal Precautions and Body Substance Isolation and applies to all patients regardless of their diagnosis or presumed infection status. Standard Precautions are designed to reduce the risk of transmission of microorganisms from both recognized and unrecognized sources of infection.

Policies:

1. Standard Precautions will be followed by all workers at Maine Medical Center.

2. Standard Precautions apply to:
   - Blood
   - All body fluids, secretions and excretions, except sweat, regardless of whether or not they contain visible blood,
   - Non-intact skin
   - Mucous membranes.

3. Wash hands after contact with blood, body fluids, secretions or excretions, and contaminated items irrespective of whether gloves were worn. Hand hygiene should take place immediately after gloves are removed, between patient contacts, and in any other situation in which hand hygiene is appropriate to avoid transfer of microorganisms to other patient or the inanimate environment.

4. Wear gloves when touching blood, body fluids, secretions or excretions and contaminated items. Clean gloves should be donned before touching mucous membranes and non-intact skin. Gloves should be changed between contact with "dirty" and "clean" sites on the same patient.

5. Mask and eye protection should be worn to protect mucous membranes during

procedures that are likely to generate splashes of blood, body fluids, secretions, and excretions.

6. Wear a gown to protect skin and clothing during procedures that are likely to generate splashes of blood, body fluids, secretions, and excretions.

7. Used patient-care equipment that is soiled should be handled in such a way as to prevent (a) exposure of other patients, visitors, or healthcare workers skin and mucous membranes to the soiled or contaminated item; (b) contamination of patients, visitors or healthcare workers clothing; and (c) transfer of microorganisms to other patients, visitors, healthcare workers, and the environment. Per policy, reusable equipment should be cleaned and reprocessed appropriately before use with another patient.

8. Routine care, cleaning and disinfection of environmental surfaces including beds, bed rails and bedside equipment will occur per policy.

9. Soiled linen should be handled in such a way as to prevent skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments.

10. Sharp instruments and needles should be handled with care to prevent injuries. Needles should not be recapped. When recapping is necessary, follow Policy and never use two hands.

11. Mouthpieces, resuscitation bags, or other ventilation devices should be available in areas where the need for resuscitation is predictable.

12. Patients who contaminate the environment or who cannot assist in maintaining appropriate hygiene or environmental control should be placed in a private room.

Reference:

Centers of Disease Control and Prevention CDC). Recommendations for Isolation Precautions in Hospitals, 1996

Original Date: 4/98

Committee(s) Approval and Date: Infection Prevention Committee 1/99, 5/00, 1/02, 2/05, 1/08, 3/11

Pet Policy

Maine Medical Center
Institutional Infection Prevention Policy Manual

Policy Title: Patient Pet Visitation

Policy Summary: It is the policy at Maine Medical Center (MMC) that pets are a source of comfort to patients. However, pets post a health risk to our patients and are not allowed in the hospital, except in certain circumstances, outlined below. As a pet visit is approved, a pass, as outlined in this policy, must be issued prior to every visit. This policy to not apply to Service Animals (Policy 703.10) or Pet Therapy Program dogs (Policy 703.9a).

Policies:

1. Personal pet is defined as "an animal for pleasure or companionship". A patient's personal pet visits are reserved for long-term or terminally ill patients. Exceptions to this policy may be approved by the unit Nursing Director for special patient circumstances. These animals may not have undergone an evaluation of the temperament and obedience; thus, there behavior with others may be unpredictable.
2. The pet must be a domestic companion animal. This excludes the following species, which may pose a higher risk of causing human injury or infection:
    a. Nonhuman primates
    b. Reptiles and amphibians
    c. Hamsters, gerbils, mice, guinea pigs, rabbits and rats
    d. Birds
    e. Other animals that are not house broken
3. Animals that have not been litter trained or for which measures cannot be taken to prevent exposure of patients to the animal's excrement cannot be brought into the hospital.
4. Visits must be preapproved by the unit's Charge Nurse and a pass must be issued by the Charge Nurse of the patient care unit before each visit. Visits will be limited to one hour in length in a designated place.
5. The animal must be under the control of an adult (at least 18 years of age) throughout the visit and the handler must have the pass ready to show, if asked. Anyone with an animal who is unable to show a preapproved pass for the correct date will be asked to leave the facility.
6. Total responsibility for the animal's actions and the results of such actions lie with the adult handler. The pet must never be left alone with the patient.
7. The pet must be taken directly to the unit and the preapproved site of visitation and then directly back out of the facility. The pet must not be allowed to interact with other patients or visitors or be taken to other areas of the facility.

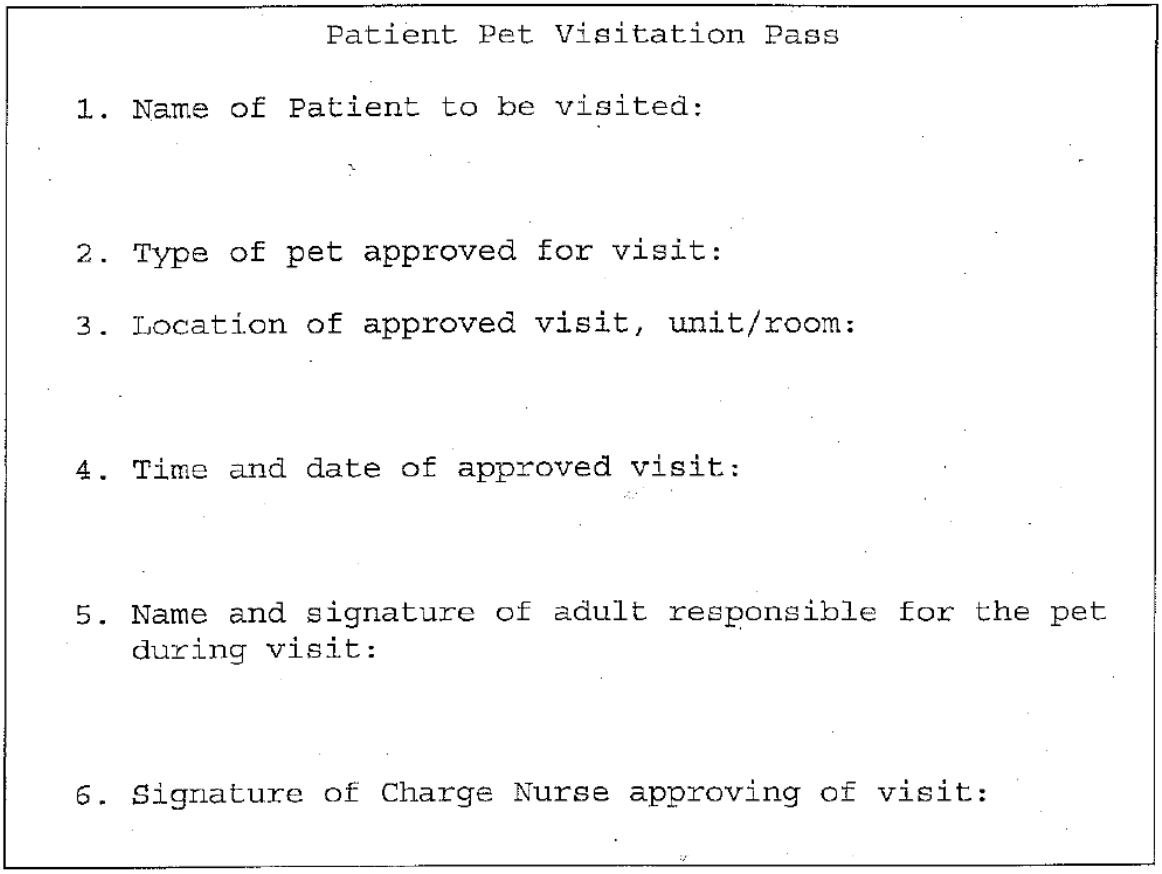
8. At any time, any member of the MMC staff may ask the handler to leave the building with the pet for the safety of patients and staff.
9. Visiting pets are not allowed in the following areas:
    a. Food preparation, storage and serving areas
    b. Areas used for cleaning/storage of human food and utensils/dishes
    c. Vehicles used for the transportation of prepared food
    d. Employees' toilet, shower, office, and dressing/locker rooms
    e. Nursing stations, drug preparation areas, sterile and clean supply rooms
    f. Linen storage areas
    g. Areas where soiled or contaminated materials are stored or processed
    h. Sterile procedure areas such as the OR, cardiac catheterization lab or interventional radiology
10. The animal must not pose a threat or nuisance because of size, odor, disposition, or behavioral characteristics. The pet must be on a short leash or in a carrier. Use of a retractable leash is not allowed.
11. The animal must not be a current resident of an animal shelter, pound or similar facility and must have been in the home permanently for at least 6 months.
12. The animal must be at least 1 year old.
13. The animal's intake of food and water should be restricted within 2 hours of the visit. The family is responsible for walking the animal, if necessary, prior to the visit. The handler must pick up the elimination in a plastic bag and deposit it in the trash. Hands must be washed before entering the facility.
14. The animal must not have been fed raw foods of animal origin within the previous 90 days.
15. The animal must have been bathed within 24 hours before the visit. The animal must have clean ears and short nails.
16. The animal must be healthy and current with immunizations, including rabies vaccination. The animal must be free of communicable diseases and parasites and be on a flea control program. The animal must be free of any skin condition or wounds.
17. Handlers must ensure that the pet does not lick or come in contact with the patient's open wound or devices.
18. If an animal is allowed in a patient's bed, a barrier such as a disposable towel or sheet should be placed between the animal's coat and the patient's linen. The barrier should be removed and sent for cleaning or discarded when the animal leaves.
19. When the visit is finished, the patient must wash his/her hands or use an alcohol-based hand sanitizer. Assistance will be provided by the patient's nurse if the patient is unable to accomplish this independently.
20. Employees are not allowed to bring a pet to work, which includes leaving a pet in their vehicle or bringing the pet into any MMC building.

Procedures (Responsibility of the Patient Care Unit):

1. Discuss the request with the patient and family

2. Evaluate the situation surrounding the request for the visit. Visits should be limited as described above.
3. If the visit is approved, complete the pet visitation pass and issue it to the family member who will be bringing in the pet.
4. If the pet is brought in without a pass, inform the visitor of the policy and ask him/her nicely to leave until a visit can be prearranged for another time.

Example:



Patient Pet Visitation Pass

1. Name of Patient to be visited:

2. Type of pet approved for visit:

3. Location of approved visit, unit/room:

4. Time and date of approved visit:

5. Name and signature of adult responsible for the pet during visit:

6. Signature of Charge Nurse approving of visit:

References:

- JCAHO Reference Standard IC4.10
- Association of Professionals in Infection Control and Epidemiology Text, Chapter 68, pp. 1-8.

Original Date: 4/98

Committee Approval and Date: Infection Prevention Committee 5/00, 1/02, 2/06, 1/08, 7/10, 3/11, 3/14

Airway Clearance Policy

MAINE MEDICAL CENTER
INSTITUTIONAL POLICY MANUAL

Policy Title: **Airway Clearance -** Adult / Pediatric

Policy Summary: It is the policy of Maine Medical Center (MMC) to assess and address the airway clearance needs of our patients using appropriate techniques and medical devices.

Policies:

1. Licensed (RN/LPN, PT, RT) clinicians may perform various airway clearance techniques or utilize appropriate medical devices for the purpose of airway clearance.

Procedures:

1. Perform and document baseline assessment of lung sounds, respiratory rate and characteristics.
   a. Assess breath sounds via auscultation and the ability to clear secretions
   b. Determine the rhythm, depth of breathing, and rate.
2. For airway clearance techniques including percussion, vibration, and directed coughing procedures see Appendix A. Airway Clearance Techniques and Breathing Exercises
3. For medical devices used to mobilize pulmonary secretions see Appendix B. Guidelines for Use of Airway Clearance Devices.
4. Assess effectiveness of treatment. Document lung sounds, respiratory rate and characteristics, secretions produced and patient tolerance to the airway clearance techniques or use of medical devices.

References:

Frownfelter, D. & Dean, E. (2012). Cardiovascular and Pulmonary Physical Therapy: Evidence and Practice, 5th Ed., Mosby Elsevier, St. Louis.

Hillegass, E. (2017). Essentials of Cardiopulmonary Physical Therapy, 4th Ed., Elsevier Saunders, St. Louis.

Strickland, S.L., Rubin, B.K., Drescher, G.S., Haas, C.F., O'Malley, C.A., Volsko, T.A., Branson, R.D., and Hess, D.R. (2013, December). American Association for Respiratory Care Clinical Practice Guideline: Effectiveness of Nonpharmacologic Airway Clearance Therapies in Hospitalized Patients. *Respiratory Care 58* (12): 2187-2193. https://www.aarc.org/wp-content/uploads/2014/08/nonpharmacologic_2013.pdf

Original Date: 2001

Committee(s) Approval and Date:

Institutional Policy Review Committee:9/18/17

Online Resources

GENERAL

Cystic Fibrosis Foundation www.cff.org
Clinical Trials Finder www.cff.org/Trials/Finder
Northern New England CF Consortium website www.nnecfc.org

VASCULAR ACCESS DEVICES

Introduction: https://www.youtube.com/watch?v=EHQq_G5ITb8&feature=youtu.be
Line flushing: https://www.youtube.com/watch?v=yi7A-eZ8NUc&feature=youtu.be
Home care: https://www.youtube.com/watch?v=PmcW7r-2taA&feature=youtu.be
Dressing changes: https://www.youtube.com/watch?v=urGR0IFAxPM&feature=youtu.be

INFECTION CONTROL

Infection Prevention and Control Guideline: 2013 Update www.jstor.org/stable/10.1086/676882
Handwashing technique: https://www.youtube.com/watch?v=orUQXS4vUxo
Nebulizer cleaning: https://www.youtube.com/watch?v=jO4RuLyfrOM

SINUS DISEASE

CF Foundation Webinar: https://www.youtube.com/watch?v=j53imMOPbm8

FEEDING TUBES

Feeding tube placement: https://www.youtube.com/watch?v=bxBYi9MvuYs
Mic-Key tube patient experience: https://www.youtube.com/watch?v=f3pTK_zhkWs
Procedure pain patient experience: https://www.youtube.com/watch?v=aIwib7u5tHs

FAMILY PLANNING AND PREGNANCY

Fertility issues in males: ttps://www.youtube.com/watch?v=XZSZ2xdQfbo
Male fertility: https://www.youtube.com/watch?v=S-Rzn1KGQHg
Female fertility and pregnancy: https://www.youtube.com/watch?v=r_-M9Un0v_0

SOCIAL MEDIA

CF Virtual Events: www.cff.org/minicon
The Frey Life: https://www.youtube.com/user/thefreylife

Workflow Diagrams and Epic Tools

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Miscellaneous/Notes