Disclaimer: These guidelines are intended to be an educational guide and should never be used without proper clinical and common sense. The information in this guide is compiled from sources believed to be reliable and exhaustive efforts have been made to make the guidelines as accurate as possible—however, the accuracy and completeness of the recommendations made within are not guaranteed. Always confirm the indications and dosages of all medications in these guidelines with an independent source such as a hospital pharmacy. Medicine is an ever-changing science. The information contained in this text is subject to change without notice.

The UCSF Cystic Fibrosis Center

<table>
<thead>
<tr>
<th>Appointments</th>
<th>415-353-2961</th>
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<tbody>
<tr>
<td>Center Director</td>
<td>Dennis Nielson MD</td>
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<tr>
<td>Director, Adult CF Center</td>
<td>Mary Ellen Kleinhenz MD</td>
</tr>
<tr>
<td>Associate Director Adult CF Center</td>
<td>Steven Hays MD</td>
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<tr>
<td>CF Fellow</td>
<td>Andrea Glassberg MD</td>
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<tr>
<td>Pulmonary Fellow</td>
<td>Ask for fellow on call</td>
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<tr>
<td>CF Nurse</td>
<td>Debbie Lallas RN MS</td>
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<tr>
<td>CF Nutrition</td>
<td>Carrie Donovan</td>
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<td>CF Social Work</td>
<td>Monica Eisenhardt</td>
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<td>CF Respiratory Therapy</td>
<td>Jeff Tarnow Or ask for on call beeper</td>
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<tr>
<td>ID Pharmacy</td>
<td>Vicky Dudas Joe Guglielmo</td>
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The UCSF Cystic Fibrosis Center provides multidisciplinary care for cystic fibrosis (CF) patients under the care and supervision of pediatric and adult cystic fibrosis specialists. The UCSF Cystic Fibrosis Center is a provider of adult CF care approved by the State of California and the Cystic Fibrosis Foundation (CFF).

Adults with CF are hospitalized on the General Medical Service under the immediate care of staff physicians. Adult CF consultation and supervision are provided by Drs. Kleinhenz, Hays or Glassberg with support from the Pulmonary Consult Fellow and Attending. Dr. Kleinhenz is available for questions and issues that are not resolved after review with the Fellows.

The 2003 CFF Patient Registry Annual Data Report indicates that just over 50% of adults with CF (age 18-30 years) require hospitalization and/or a course of home IV antibiotics for an exacerbation of chronic CF sinopulmonary disease each year. It is recognized that several different processes can result in a CF exacerbations. Among them are intercurrent infection with community respiratory pathogens, acquired antibiotic resistance of the patients own “CF” respiratory flora, acquisition of new environmental pathogens such as Burkolderia or aspergillus, irritation of respiratory track by allergens, environmental tobacco smoke or other respirable agents and finally, a failure of the patient to maintain good CF care. The root cause of the patient’s decompensation should be sought to better understand the illness and address problems. Other CF-related pulmonary complications which may prompt hospitalization include: pneumonia, respiratory failure, hemoptysis or pneumothorax. On rare occasions, patients require a “tune-up” of their CF regimen to reverse insidious progression of respiratory dysfunction. CF is a multi-organ, disease; GI and
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hepatobiliary disease, CF related diabetes mellitus (CFRD) or drug desensitization lead to admission or complicate a CF exacerbation. Examples of common, serious CF morbidities include: distal intestinal obstruction syndrome, intestinal perforation, appendicitis, cholelithiasis, biliary tract infection, acute pancreatitis, progressive liver disease, and fracture due to osteoporosis. Historically, many hospitalizations focus on initiating culture-specific antibiotic therapy for the CF pulmonary exacerbation. Data suggest that longer hospitalizations may be associated with better physiologic outcomes. Ancillary treatments available in the hospital, intensive mucus clearance therapy, frequent bronchodilator treatments, oxygen, nutritional resuscitation and physical support are not readily reduplicated in the home. Additional education about CF specific therapies provided by the multi disciplinary CF Team may contribute to improved patient outcomes with longer hospital stays.

I. THE OUTPATIENT CF REGIMEN

The multidisciplinary CF team works with CF patients and their families to design treatment regimens to mitigate the end-organ dysfunction that occurs as the consequence of abnormal or absent CFTR. Each patient should have a regimen tailored to his or her clinical needs, personal and medical resources and supportive environment. Two major components of CF care are the CF pulmonary regimen and nutritional support with particular attention to management of pancreatic insufficiency.

The outpatient CF pulmonary regimen is designed to clear the airway of abnormal mucus and reduce the density of airway pseudomonas in patients colonized/infected with this pathogen. Key elements include mucus clearance, mucolytic nebulization (PULMOZYME), and scheduled use of oral or/and inhaled antibiotics. Proven CF antibiotic therapies include azithromycin 500 mg Monday, Wednesday and Friday and TOBI (300 mg/5 ml) inhaled twice daily in cycles of 28 days on therapy and 28 days off therapy. The target of these treatments is the density of pseudomonas in the respiratory secretions. Not all adults with CF harbor pseudomonas in their mucus; this observation probably derives from the variability in CF gene mutations that occurs in adults, particularly those for whom the diagnosis of CF was delayed.

Pancreatic insufficiency (PI) occurs in 85% of CF patients. To avert nutritional deficiencies and impaired growth, CF patients with PI take enteric coated pancreatic enzymes 1000-2000 lipase units/kg/meal and snack. Most patients have a supply at the bedside. Generic preparations lack potency and are not used. Pancreatic insufficiency impairs the absorption of vitamins A, D, E and K. Vitamin supplementation is provided as ADEK vitamins bid (see UCSF Formulary for composition of this preparation with enhanced water solubility of fat soluble vitamins). If pro-time is prolonged, patients should receive 5 mg of aqueous vitamin K daily until pro-time is corrected; parenteral vitamin K may be required in some settings.

II. LABORATORY EVALUATION

The following tests inform the evaluation and treatment of adults with CF who require hospitalization. Additional tests may be necessary if complications arise. Recent outpatient studies are not necessarily repeated. Routine daily blood studies are typically not appropriate. Some of the patients articulate strong opinions about the number and frequency of tests obtained. While it is important to recognize those feelings, clinical decision making should not be compromised.

A. Blood testing:

1. Initial: Hemogram, urinalysis and chemistry panel should include electrolytes, creatinine, screen for liver disease, diabetes (random blood sugar >110 g/dL) malabsorption (albumin, pro-time, vitamin A and vitamin E levels.) Amylase and lipase may be appropriate in the setting of abdominal discomfort.

2. Serial: Creatinine is monitored approximately every 3 days if receiving aminoglycosides. CBC is repeated if the initial hemoglobin suggests anemia (Hbg <10 g/dL) or the admitting WBC showed neutropenia. There is usually no indication for daily lab work.
3. **Arterial blood gases:** Obtain ABGs when the O2 saturation on room air is < 93%, the serum HCO3 is elevated, the patient is severely ill, complains of morning headaches or if there is evidence of cor pulmonale.

4. **Immunoglobulin E (IGE)** is the best predictor of allergic bronchopulmonary aspergillosis and may be useful when a patient not responding to treatment as expected.

5. **Genetic screening:** Ideally, gene mutation analysis should be available on all patients. The CF Team will inform you of the need to obtain DNA testing for cystic fibrosis mutation analysis. UCSF offers a standard panel screening for 30 common mutations; Ambry Diagnostics screens for > 100 mutations and is also available.

**B. Cultures:**

1. **Sputum culture and sensitivities** should be obtained on each admission unless obtained within the previous week. Requisitions must indicate the patient has **cystic fibrosis.** This affords special processing to isolate *S. aureus* (mannitol salt agar plate is used) and *Burkholderia cepacia.*

2. **Sputum for fungal stain and culture.** *Aspergillus* is an important organism in CF as it may cause mycetomas or allergic bronchopulmonary aspergillosis. Other fungi have been reported in CF secretions and may contribute to clinical instability and important decisions about lung transplantation candidacy.

3. **AFB culture** should be requested at least once/year because of the increasing incidence of atypical mycobacterial infections in CF centers (about 20%). It is likely that the abnormal CF gene mutation is a risk factor for acquisition of *M. avium intracellulare.*

4. **Blood cultures** are usually **not** indicated except for patients with high fevers, sepsis syndrome or suspected indwelling catheter infection.

5. **Sinus cultures** should be obtained if there is evidence of sinusitis by clinical examination or sinus CT scan. A discordance in the antibiotic sensitivities and the microbial flora of the upper and lower respiratory tract has been observed in CF patients and influence decisions about antimicrobial drugs and duration of treatment.

**C. Imaging:**

1. **Chest x-ray** should be obtained on admission (or the next morning if patient not very ill). For patients with advanced CF pulmonary disease, pneumonia or atelectasis may be inapparent on the PA and lateral chest films. **Chest CT scans** should be considered whenever there is discordance between the patient’s clinical status and changes seen on the chest radiograph.

2. **Screening sinus CT** with coronal views may be useful if nasal complaints are significant or if ENT consultation is planned.

3. **KUB** and flat plate of the abdomen may be helpful regarding extent of constipation.

4. **Abdominal ultrasound** is useful for abdominal pain (e.g., for gallstones).

**D. Pulmonary function:**

1. **Spirometry** may be ordered within in 24 hours of admission (unless performed in the clinic just before admission) to serve as a baseline to assess response to treatment. Preferably this should be performed by the Pulmonary Function Laboratory (x6-2995) so that it is entered into the STOR system. Repeat spirometry should be obtained at the end of treatment either as in or outpatient to assess clinical response and help guide future decision making.

2. **Arterial blood gases** may suggest shunting; shunts can be measured in the PFT lab.

3. **Complete physiologic tests of lung function** including body plethysmography (body box) with measurement of lung volumes and DLCO should be obtained annually. Complete PFTs are best obtained in they ambulatory setting when patient’s lung function is optimal. CF pulmonary disease is progressive over time; the average annual loss of FVC is approximately 60 cc. For CF
patients, “lung function is destiny” meaning that respiratory failure remains the leading cause of death in CF. Thus, declines in lung function should prompt re-evaluation of patient regimens in the hope of recovering function or stabilizing the rate of decline.

4. Exercise testing is sometimes requested to assess oxygenation and ventilatory reserve. This provides important additional information about the severity of the respiratory impairment, oxygen needs and the need for exercise training.

III. RESPIRATORY CARE

A. Mucus Clearance Therapy:

While CF patients practice mucus clearance once or twice daily as part of maintenance CF therapy, patients who are hospitalized for respiratory exacerbations require more aggressive therapy. A form of mucus clearance therapy should be administered 4 to 2 times daily by Respiratory Care Service. To accomplish this goal, order a CF Respiratory Care Assessment. The experienced RT staff will perform a comprehensive evaluation of the patient and plan for the mucus clearance, arrange aerosol therapies and provide oxygen as needed.

UCSF Respiratory Care services surveyed adult CF patient treatment preferences and learned that effective, preferred treatments are: PEP therapy, the therapy vest and IPV. An array of other treatments can be explored once the patient has improved. The respiratory care practitioner may advise you which modality is best for the individual patient. Providing frequent, effective mucus clearance early in the treatment course promotes physiologic stabilization and symptomatic relief.

PEP (positive expiratory pressure with a mouthpiece.) uses a simple, disposable device based on the premise that positive pressure at the mouth will force air through the pores of Kohn behind plugged airways. This device may be used alone or in series with the nebulizer.

ThairAPY Vest provides whole chest vibration. The vest is inflated and deflated with compressed air; the frequency of the cycles can be adjusted. Increasing numbers of UCSF Adult CF patients use the “Vest” as part of their home regimens.

Intrapulmonary oscillator (IPV) use a modification of classic positive pressure ventilators to oscillate of the air column under pressure of compressed gas.

There are 2 oral oscillatory or vibratory therapy (Flutter, Acapella) which are simple, portable, relatively inexpensive devices that the patient can use at home, in the car, etc. The acapella valve can be fitted to the compressor and used in series with nebulized medications.

Classical physiotherapy and postural drainage (CPT) combines clapping of the external chest wall to create vibration and positioning the lobar bronchi against gravity to clear mucus. This is a labor intensive therapy in the hospital and even when performed well, may not be as effective as the other treatments. It is the first form of mucus clearance therapy CF patients experience and many of the patients enjoy the physical contact. In some patients with lobar atelectasis, CPT may be added to other forms of mucus clearance. CPT may aggravate hypoxemia and GERD.

Mucus clearance is applied with caution in the setting of hemoptysis.

B. Inhaled Bronchodilator Therapy:

Bronchodilators are clinically helpful in most patients admitted for treatment of CF. Nebulized albuterol (0.5-1.0 ml) or xopenex (1.25mg.dose) usually combined with unit dose ipratropium in 2-3ml of normal saline, is given every 4-6 hours.

Meter dose inhaler treatments allow the patient autonomy in their care. Transition to MDIs may be recommended by the Respiratory Care Service, both to improve patient independence and to prepare
Inhaler technique should be specifically taught by the respiratory care practitioner or by the medicine clinical pharmacy service. Most patients do better with addition of a spacer device (e.g., Aerochamber).

Intuitively, long-acting beta₂ agonist or anticholinergic treatments {salmeterol (Serevent™) by discus, famoterol (Foradil™) aerolizer and/or tiotropium (Spiriva™)} may have a role in CF management although these agents have not yet been studied. Beta₂ agonist or anticholinergic MDIs have been studied and appear to benefit CF patients with airway responsiveness.

Treatment with airway anti-inflammatory drugs is important if there is a concurrent diagnosis of asthma/allergic airway disease. The discus products combining salmeterol with fluticasone have appeal with the reduced dosing frequency; three dosage forms are available each containing 50 mcg of salmeterol plus 100, 250 or 500 mcg of fluticasone per dose (Advair 100/50, 250/50 or 500/50). Theophylline has no established role in CF care. It has narrow therapeutic index and has a weak bronchodilator effect.

C. Mucolytic therapy:

Pulmozyme is an important CF therapy with its use validated in controlled clinical trials. It is a cornerstone of CF respiratory management. Pulmozyme increases expiratory flow volumes and increases the interval between infectious pulmonary exacerbations. Recombinant human Dnase (Pulmozyme) is given as an aerosol once or twice daily. Pulmozyme is not mixed with other aerosol medications and is not given by IPV. Hypertonic saline: New evidence supports the use of hypertonic saline in concentrations ranging from 3 to 7% as a low cost mucolytic. Some patients may experience bronchoconstriction that can be mitigated by pretreatment or admixture of a beta2-agonist drug.

D. Oxygen therapy:

This is appropriate for CF patients to keep SaO₂ > 90% both awake and asleep. Intrapulmonary and intracardiac shunting should be considered when patients require high FiO₂ early in the clinical course or need supplemental oxygen with only moderate CF lung disease. The prevalence of patent foramen ovale is at least that in the general adult population (1 in 4) and may be higher in patients with CF. Shunting can be evaluated in the PFT lab and with a TTE with bubble study.

Arterial blood gases and overnight recording of oximetry (available through the Pulmonary Service) are indicated when there is significant hypoxemia (O₂ saturation <94% at rest), cor pulmonale, or if long term oxygen therapy is under consideration. PaCO₂>45 mmHg is abnormal and indicates hypoventilation or respiratory failure. Transitory hypercapnea is observed and improves with the treatment of CF lung disease. Many patients with severe CF lung disease require noninvasive ventilation with sleep or a nearly continuous basis as a bridge to lung transplant.

IV. ANTIBIOTICS IN CF

From an early age, patients with CF are prone to respiratory infection, clear these infections more slowly and are predisposed to acquire bacteria from the environment. As a result, antimicrobials are an important part of CF patient care and are used in three ways:

1. To treat sinopulmonary exacerbations of cystic fibrosis
2. To prevent exacerbations due to increased density of bacteria particularly pseudomonas
3. To sterilize the airway after an initial infection by pseudomonas.
In the setting of a CF sinopulmonary exacerbation, antibiotic therapy should be driven by the results of cultures. Empiric antibiotics selections may be based on previous culture reports; recent studies indicate that patients tend to be infected by the pathogens that colonize their airways. Final antibiotics decisions should derive from a culture obtained no more that 7 days before hospitalization. *Pseudomonas* is generally treated with two drugs of different classes. When multiple morphotypes are identified (e.g., of *Pseudomonas*), try to find at least one drug for each. *S. aureus* and other bacteria more typical of community acquired respiratory pathogens are generally treated with single agents. If recent sputum cultures and sensitivities are not available, empiric therapy to address community respiratory pathogens including *S. aureus* and *Pseudomonas aeruginosa* is appropriate pending culture results.

Antibiotic dosing is predicated on enhanced excretion of most antibiotics; this is attributed to the abnormal CFTR and other factors. Consequently, greater doses are required to achieve therapeutic levels of aminoglycosides. In general, the activity of aminoglycosides, such as tobramycin, is dose-dependent, i.e. peak levels/MIC are a better predictor than time above MIC. CF patients are not immune to aminoglycoside renal and ototoxicity; drug levels are followed to minimize these complications. Similarly, increased doses of beta-lactams and fluoroquinolones are recommended. In contrast to aminoglycosides, time over the minimum inhibitory concentration (MIC) is the best predictor for outcome with beta-lactams, such as piperacillin and ceftazidime. Dosing regimens for the commonly used antibacterial agents are listed below. ID Pharmacy (719-9421) can provide valuable assistance with respect to antibiotic dosing.

**Antimicrobial Dosing in CF (assuming normal renal function)**

<table>
<thead>
<tr>
<th>Antibiotic</th>
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<tr>
<td>Tobramycin</td>
<td>10 mg/kg IV q24h <strong>plus</strong></td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>50 mg/kg IV q8 h <strong>or</strong></td>
</tr>
<tr>
<td>Cefepime</td>
<td>50 mg/kg IV q8 h <strong>or</strong></td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>100 mg/kg/piperacillin IV q6 <strong>or</strong> i.e. 50 kg patient Zosyn 5.625g IV Q6h</td>
</tr>
<tr>
<td>Imipenem</td>
<td>20 mg/kg/dose. IV q6 h</td>
</tr>
</tbody>
</table>

If anaphylaxis to β-lactams: Aztreonam 50 mg/kg IV q6h

Possible alternative to tobramycin:

| Ciprofloxacin               | 400 mg IV q8h or 750 mg PO BID [not weight based] |

Preventive use of anti-pseudomonal antibiotics derives from the view that the primary feature of CF pulmonary disease is gram negative bacillary endobronchitis, typically caused by *pseudomonas*. Due to structural lung disease, abnormal mucus and other factors that increase the susceptibility of the CF lung to infection, the goal is not to “cure” the infection but to decrease the microbial burden in the airway. A lower density of pseudomonas has been associated with objective increases in measures of lung function. An indirect benefit may be reduced production of virulence factors by microbial pathogens. *Both TOBI and azithromycin therapies fall into this class of antibiotic use in CF*. Nebulized TOBI achieves concentrations of tobramycin in the distal airways that exceed concentrations safely achieved by the intravenous route. Clinical studies have shown concentrations of tobramycin in bronchoalveolar lavage that exceed typical MIC of *pseudomonas*. Azithromycin has been shown to improve lung function and increase the interval between infectious CF exacerbations in CF patients infected/colonized by *P. aeruginosa*. The basis for this effect is uncertain; direct anti-inflammatory effects and inhibition of drug resistance genes are among the mechanisms under consideration.
The application of antibiotics to rid airways of *pseudomonas* after its initial recovery in sputum cultures is the subject of 2 multicenter clinical trials.

A. **Anti-pseudomonal antibiotics:**

Pending the results of microbial sensitivities, two anti-pseudomonal drugs are selected by recent microbial sensitivities. Renal clearance and the volume of distribution of antibiotics are both increased in some CF patients; this fact results in unusually large doses.

B. **Multi-drug resistant (MDR) pseudomonas:**

Effective treatment of pseudomonas may be devised despite apparent complete drug resistance. Synergism studies may be obtained on CF patients at no charge through the Microbiology Laboratory (353-1268) but results will not be available for the current hospitalization (as they are sent to Columbia University in New York.) Colistin is suggested as an approach to MDR pseudomonas however colistin has a narrow therapeutic index. Parenteral therapy with this agent will be initiated only after consultation between the CF Team and the ID Pharmacy Service. There may be a role for azithromycin therapy in patients with MDR *P. aeruginosa* although this situation has not been specifically studied. Anecdotal reports suggest a possible additive role for chloramphenicol and rifampin in MDR pseudomonas, but controlled data are lacking.

The ID Pharmacy service is available to help design and supervise antibiotic regimens for patients with MDR Pseudomonas.

C. **Burkholderia cepacia** is resistant to multiple drugs and susceptibility testing should be checked for each isolate.

D. **Staphylococcus aureus** is an important CF respiratory pathogen in infancy and adolescence. Its recovery is eclipsed by the emergence of *pseudomonas* and special microbiology techniques are utilized with CF respiratory specimens to allow its identification. In the hospital, parenteral nafcillin or vancomycin are the preferred agents. Doses for intravenous therapy are:

- **Nafcillin** 50 mg/kg q 6 hours (200 mg/kg/day)
- **Vancomycin** 15 mg/kg q 12 hours (30 mg/kg/day)

*MRSA is an increasing problem in CF; MRSA can be acquired in the hospital or the community as in normal hosts. Vancomycin is appropriate for situations where the patient is known to have had MRSA infection/colonization or serious S. aureus infection (pneumonia) in the setting of penicillin allergy. For mild disease, doxycycline can be used.*

E. **Antibiotic blood levels:**

1. Studies in CF support once daily dosing with tobramycin. The tobramycin trough level should be measured just before 2nd dose. Levels < 1.0 mcg/ml are desired. However, patients with any level of renal insufficiency are candidates individualized dosing. The medicine service clinical pharmacist or infectious disease pharmacist should be consulted with questions regarding tobramycin levels outside the desired range.

**EVERY CF PATIENT WILL HAVE A TOBRAMYCIN TROUGH LEVEL DRAWN AND REVIEWED BEFORE DISCHARGE ON IV TOBRAMYCIN. IF THE TROUGH LEVEL IS MISSED BEFORE THE 2ND DOSE, CATCH IT BEFORE THE 3RD OR 4TH DOSE.**
2. For vancomycin, only trough levels are necessary, and they should be in the 10-15 mcg/ml.

F. Antibiotic assistance:
If there are questions about choice of antibiotics or dosing guidelines, an Infectious Disease Pharmacist is available 7 days a week (719-9421).

G. IV access:
Peripheral IV lines may be used initially, but most patients should receive intravenous antibiotics via a central line, either a percutaneously inserted central catheter (PICC) or an indwelling port. PICCs are usually placed by the PICC line nurse (3-8790) once it is clear that the patient will need > 7 days of parenteral therapy. Choice of IV access method must be determined by multiple factors including: age, previous experience of the patient and caregivers, expected length of therapy and anticipated frequency of future IV therapy. The risk of a long term “foreign body” (e.g., PORT) must be weighed against the disadvantages of repeated PICC placement.

H. Inhaled antibiotics:
Inhaled tobramycin 300 mg/5cc in preservative-free saline is marketed at TOBI® and is an approved CF therapy for the prevention of pseudomonas related pulmonary exacerbations. When patients are admitted to the hospital for other reasons and they are in a month on TOBI, they should continue this therapy with their supply of TOBI from home. TOBI is administered as nebulization therapy BID in cycles of 28 days on therapy and 28 days off therapy; the Pari LC Plus nebulizer is the approved device. TOBI is well tolerated over the range of lung function seen in adult with CF. TOBI is NOT typically used for treatment of CF exacerbations. Simultaneous administration of tobramycin by inhaled and intravenous routes may be associated with increased toxicity. Lower doses of tobramycin do not have a role as inhaled therapy for CF.

Inhaled colistin (150mg /10 cc sterile water) can be an effective adjunct in patients infected by non-pseudomonas, gram negative bacilli. Colistin is administered BID and is well tolerated by most patients.

I. Home IV antibiotics:
Courses of IV antibiotics may be completed at home. The enthusiasm for abbreviated hospitalizations with home antibiotics is decreasing with some CF Centers showing better clinical outcomes as patients spend more time in the hospital. **Home IV therapy can be considered when the patient is reliable; there is objective evidence of clinical improvement and access to the other measures needed to resolve an exacerbation will continue.** If home IV antibiotics are contemplated, contact Home Care 24 hours prior to discharge. If there are major logistic problems, Home Care will help you work them out in advance (e.g., IV pump, choice of lines, how many antibiotics). It is usually not possible to give more than 2 antibiotics IV at home, and antibiotics should not be given more often than every 8 hours unless the patient has a computerized pump. The CF TEAM will help the ward team assess whether home IV therapy will work for the individual patient and family. Psychosocial as well as medical factors must be considered. The patient’s ability to comply with regular dosing and line care is crucial for the success of home therapy. An adequate home environment includes electricity, refrigeration and a working phone.

Selection of patients for home intravenous antibiotics is sometimes difficult. Pressure to free up hospital beds makes this decision even more difficult. The following checklist can help in the decision making process:
• an acceptable form of IV access can be achieved and maintained;
• clinical response to initial therapy appears adequate;
• the sputum has been processed and drug sensitivities are known
• antibiotics are revised to reflect microbial susceptibilities
• no allergic reaction to drugs (or, controlled after inpatient desensitization)
• an acceptable home care/nursing company has been identified;
• the home setting is appropriate;
• increased mucus clearance and bronchodilator therapy can be maintained
• oxygen can be provided if needed
• no uncontrolled CF complications (e.g., diabetes) are present.

Unfortunately, financial issues must also be considered. Not all third party payers will pay for home antibiotics. In occasional cases, one may consider skilled nursing facility (SNF) placement for completion of antibiotics. Multi-resistant organisms and inability to receive chest physiotherapy may make that choice less appealing. It is also difficult for young people who are otherwise fairly well to accommodate to care in a SNF even for 3-6 weeks.

J. Monitoring of home antibiotic therapy

Most home care companies have policies related to oversight of home infusion therapy. For patients with serum creatinine levels less than 1.2 and an appropriate trough tobramycin or vancomycin level, further testing is not required unless the course of antibiotics extends beyond 21 days.

V. NUTRITIONAL GUIDELINES AND BOWEL CARE

Weight loss is common in CF patients so nutritional assessment and therapy are integral parts of hospitalization.

A. Diet:

Unrestricted, general diet should be ordered with regular snacks and nutritional supplements. As a rule, the more calories are better. Dietary consult should be requested routinely for CF patients. The nutritionist will assess energy and protein needs, review appropriate lab studies (e.g., CBC, vitamin levels, albumin, pre-albumin), and determine the need for a calorie count. Consideration is given to temporary or chronic tube feeding in patients with BMI less 19. Tube feeding is given serious consideration in patients with end stage disease who may be too debilitated or dyspneic to meet their daily requirements. This is particularly true for patients seeking lung transplantation. Tube feeding is not without risk and there are no well-established protocols to guide this intervention in the adult CF population.

B. Check body weight and admission and every 3-5 days daily to guide nutrition.

C. Diabetes:

If diabetes is present, it is managed with oral hypoglycemics or insulin and not by caloric restriction. CF patients with diabetes benefit from a plentiful carbohydrate consistent diet.

D. Pancreatic enzyme replacement:

See CF regimen for comments on the prevalence of PI in CF. Keep a supply of pancreatic enzymes at the bedside. The usual dose for adults is 4-6 Pancrease MT-16 capsules (16,000 units lipase/capsule) or equivalent just before meals or snacks, though there is some variability. The dose should be adjusted to normalize bowel movements, relieve constipation and assist with weight gain. Several CF Centers check random stool specimens for neutral fats and fecal elastase 1 as an objective way to assess the adequacy of enzyme supplementation.

F. Vitamin supplementation: see above

G. GERD and gastric hyperacidity:
The extent of upper GI involvement in adults with CF is not fully understood. Preliminary data indicate a high prevalence of GERD. Gastric hyperacidity may lower the pH in the duodenum and inactivate exogenous pancreatic enzymes despite the enteric coating. Empiric treatment is appropriate for patients with symptoms; asymptomatic patients may warrant a 24 hour pH probe study and/or EGD.

H. Bowel Motility:

Bowel motility problems are common in adults with CF. Late recognition of CF, meconium ileus surgery, poor control of pancreatic insufficiency and CFRD may predispose to motility problems. Severe constipation is one manifestation and may present as distal intestinal obstruction syndrome (DIOS) or "meconium ileus equivalent". Stool-filled bowel may be palpable in the right or left lower quadrant. The key to long-term management is adequate intake of pancreatic enzyme supplements and use of Proton pump inhibitors PI. Temporarily Fleet's enemas or Go Lytely (4 liters by mouth over a couple of hours) are of help. In more severe cases a Gastrografin (high osmotic load) enema may be effective; this may be scheduled like a barium enema or may be given on the floor. The usual procedure is to mix 480 ml. of Gastrografin with saline to make 1 L. and administer like a regular enema with retention as long as is comfortable. Patients with bowel motility problems may benefit from GI consultation.

VI. POST HOSPITAL CARE

Patients do best when they provide the ward team with a successful return demonstration of treatment plans. The Adult CF TEAM will work with the ward staff and HOME CARE to provide patients with an explicit therapeutic regimen. The Adult CF Center will try to see every patient within 14-21 days of hospital discharge. Appointments may be made by calling the Chest Faculty Practice at 353-2961 (direct line 353-2244). If there are problems obtaining after hospital appointments to the Adult CF Center, please contact Debbie Lallas (476-9280) or Mary Ellen Kleinhenz, M.D. (719-7505). Ideally patients should be seen in the Adult CF Center near the completion of the antibiotic or post hospital treatment to verify that the patient is improved, the goals of treatment have been accomplished and that the patient’s CF regimen is optimized. A copy of the discharge summary should be sent to the Adult CF Director.

VII. EMERGENCIES

A. Massive hemoptysis:

Massive hemoptysis defined as 500cc/24 hrs is a life-threatening emergency managed in the ICU. Patients may require protective intubation and urgent bronchoscopy to lateralize the side of bleeding. Bronchial artery embolization of the bleeding vessel by Interventional Radiology is the usual approach to massive hemoptysis in CF. Very rarely, surgery to remove the affected lobe is done. This complication occurs in patients with severe CF lung disease (FEV1 ≤ 34% predicted.)

Minor hemoptysis is a frequent problem normally managed with antibiotics and avoidance of chest percussion. Sub-massive hemoptysis is rare and usually responds to conservative management with antibiotics; the volume of hemoptysis may dictate ICU management. In minor and submassive hemoptysis, infection is thought to inflame the lung adjacent to hypertrophic bronchial vessels and provoke bleeding; hence, the role for antibiotics. In patients with massive hemoptysis, infection may play a role but other factors like cough or increased intrathoracic pressure with valsalva maneuvers also contribute.

B. Bowel obstruction:

Partial obstruction due to "meconium ileus equivalent", usually at the ileocecal junction, is not rare. Conservative bowel hygiene measures will usually prevent complete bowel obstruction. Go Lytely, a
non-absorbable solution acting like an osmotic agent, may stimulate evacuation. Four liters is given by mouth over a 2 hour period; 240 cc is drunk every 10 min. until finished or until rectal effluent is clear. Rapid drinking of each portion is preferred to drinking small amounts continuously. In occasional cases diatrizoate meglumine (Hypaque, Gastrografin) enema is useful both to outline the extent of obstruction and to relieve it (its hypertonicity draws water into the gut). Very rarely is surgical resection appropriate.

C. Respiratory failure and end of life decisions: Most patients with CF eventually die of respiratory failure. Rarely does this occur acutely and without prior discussion. The issues of ICU transfer and intubation with mechanical ventilation will be dealt with on a case-by-case basis. Hopefully this issue will be addressed by The Adult CF Team involved before it becomes an emergency situation. The Adult CF Team should be involved in any discussion of Code Blue status. If an unanticipated emergency arises, patients should be treated aggressively, including mask ventilation or intubation with mechanical ventilation if necessary.

VIII. LUNG TRANSPLANTATION
Lung transplantation is a viable option for most patients with end stage lung disease due to cystic fibrosis. Keys to transplantation are ability to be adherent to a complex medical regimen and the availability of social support and reliable caregivers because of the tremendous physical and emotional demands both before and after transplantation.

GHPP, the major insurer for CF patients in California, covers this operation either at UCSF or at Stanford. Patients have many questions and you can use their time in the hospital to initiate the evaluation. You may call the Lung Transplant Coordinator at 476-3053 and ask her to see the patient and provide introductory materials. In some cases, you may want a formal Lung Transplant Consultation: Dr. Kleinhenz and Dr. Hays are members of the Medical Lung Transplant Team and will be pro-active in assessing transplant candidates.
A new system for lung allocation will be implemented in May 2005. The traditional consideration of accrued time on the transplant list will be superceded by an approach that includes acuity of physiologic decompensation and underlying diagnosis. The Adult CF Center works directly with the Lung Transplant Team to assure the timely listing of CF patients.

IX. PATIENT EDUCATION
Hospitalization represents an important opportunity for the CF patient and the Adult CF Center. Patients have the opportunity to update their knowledge of proven CF therapies and work with the CF TEAM. This assures access to the appropriate and best treatments for them. As patients with CF live longer, more medical specialties will join in the care of adults with CF; patients and caregivers will come to understand spectrum of clinical CF in adults goes beyond the respiratory system. This is particularly true for hepatobiliary disease and GI problems. When the CF decompensation results from a failure of adherence, the hospital setting and personnel allows the CF TEAM the opportunity to tease apart the issues and work towards an improved collaboration with patients.

This version of the “Adult CF Treatment Guidelines” represents a collaborative effort of all the disciplines represented on the UCSF Adult CF Team. The Adult CF Team acknowledges the work of Michael Stulbarg, M.D. in creating and updating earlier versions of this document. Michael is missed by his patients and
X. REFERENCES


