Cystic Fibrosis: Pulmonary Exacerbations Management Guidelines

Inclusion Criteria:
- Age ≥ 1 year with cystic fibrosis admitted for a pulmonary exacerbation.

Exclusion Criteria:
- ICU Admission
- Newborn with meconium ileus
- Admission for initiation of insulin therapy without pulmonary exacerbation
- It is at the pulmonary attending discretion to include in the protocol if the primary reason for admission is bowel obstruction, appendicitis, other acute GI condition, sinus surgery, or acute bronchiolitis.

Step 1: Admit
- Plan to admit to hospital for pulmonary exacerbation
- If from clinic, call extension 631-444-1911 to notify Transfer Center of admission.
  - Notify resident team and inpatient attending with general plan and choice of antibiotics.
- Isolation
  - ALL CF patients are to be placed on CF contact precautions on admission, regardless of organisms or symptoms per the CF infection control guidelines.
  - If droplet or airborne precautions are indicated due to the nature of a suspected infection or organism, these may be added as well.

Step 2: Plan for IV Access
- Determine type of IV access (PIV, PICC, PORT)
- Consult Special Procedure Unit for PICC placement
- If patient has a history of prior thrombus requiring enoxaparin (Lovanox) or if patient has difficult PICC placement in past, request placement by interventional radiology (IR)
- If PICC placement unavailable within 6 hours have a PIV placed for initiation of therapy.

Step 3: Initiate Therapy (use CF PowerPlan)
- Health status
  - On admission: height, weight, BMI, vitals, pulse oximetry
  - Spirometry ≥ 5 years old, if not done as outpatient
  - Routine respiratory assessment (cough, work of breathing, sputum quality and color)
  - Repeat weight should be done three times a week during admission on Mondays, Wednesdays and Fridays.
- Labs
  - Check results of last CF Respiratory culture
    - If not done in past 1 month, send a CF Respiratory culture (sputum if able to expectorate or oropharyngeal cough swab if unable to expectorate)
If AFB culture has not been done in past 1 year and patient is able to expectorate sputum, sent AFB culture and smear
- Annual labs if not done in past year.
- CF-related diabetes screening for patients ≥10 years old

- Radiology
  - Chest radiograph

- Airway clearance
  - Four times daily
    - Choice is largely based on age, patient preference/adherence, safety and MD assessment (Flume 2009)
    - Typically method of airway clearance is the same as used at home and includes high frequency chest wall oscillation therapy.
    - May need to modify airway clearance for hemoptysis, chest tubes or pneumothorax.

- Nutrition
  - CF Diet: High calorie, extra fat
  - Supplementation if indicated (enteral or oral)
  - Nutrition Consultation
  - Three times per week weights on Mondays, Wednesdays and Fridays

- Medications
  - Antibiotics (use CF PowerPlan)
    - Choice of antibiotics is based on respiratory cultures and sensitivities and patient history of tolerance and improvement
    - If using nephrotoxic medications, monitor for side effects with troughs and weekly creatinine measurements.
  - Steroids if indicated
  - Home medications

- Consults
  - Nutrition, Social Work, Case management, Child Life, Physical therapy
  - Endocrinology if patient has CF-related diabetes
  - Otolaryngology, Surgery, and others as needed.

- Begin Discharge Planning
  - Begin teaching
  - Review criteria for transition to home to complete therapy.

**Step 4: Continue Therapy and Assess for Improvement**

- Therapy
  - Antibiotics
  - Airway Clearance
  - Routine Respiratory Assessment
  - Routine Nutritional Assessment

- Assessments
  - Weights on Mondays, Wednesdays and Fridays
  - Spirometry if ≥ 5 years of age at 1 week after initiating therapy and weekly thereafter.
  - Weekly monitoring of kidney function with weekly serum creatinine
Weekly monitoring of antibiotic toxicity and/or therapeutic range with weekly troughs and/or peaks

- Elevated Glucose
  - If any fasting glucose is $\geq 126$ mg/dl or any post-prandial $\geq 200$ mg/dl, continue to monitor for a total of 72 hours.
  - If levels remain elevated, consult endocrinology

- If not clinically improving, the following options should be considered
  - Adjust/change antibiotics
  - Consider steroid burst
  - Adequacy of airway clearance
  - Consider other pathogens
  - Consider imaging
  - New baseline

Step 5A: Completion of Therapy at Home

- Assess criteria for possible transition to home for completion of IV antibiotics
- Prepare for Home IV antibiotics
  - Set up Home IV teaching
  - Arrange home care
  - Arrange and order outpatient labs
    - Home labs should mimic inpatient labs with weekly monitoring of renal function (serum creatinine) and weekly monitoring of antibiotic toxicities (antibiotic troughs) if applicable.
- Discharge Criteria
  - Patient and family needs for equipment, education, and training for transition home are identified and addressed.
  - The patient and family understand reasons to seek medical attention including signs and symptoms of malabsorption, respiratory distress and intestinal obstruction
  - Patient and family understand appropriate methods of respiratory treatments
  - All medications and therapies are available at home
  - Follow-up appointments are scheduled
    - CF Clinic visit at about 1 week after discharge (can also be done with Pediatric Pulmonology in other office hours).
    - Consult follow up is scheduled if necessary
    - Annual Audiology exam for patients at risk of ototoxicity.

Step 5B: Completion of Hospital Antibiotics and Discharge home

- Patient and family needs for equipment, education, and training for transition home are identified and addressed.
- The patient and family understand reasons to seek medical attention including signs and symptoms of malabsorption, respiratory distress and intestinal obstruction
- Patient and family understand appropriate methods of respiratory treatments
- All medications and therapies are available at home
- Follow-up appointments are scheduled
  - CF Clinic for 4-6 weeks after therapy complete
- Consult follow up is scheduled if necessary
- Annual Audiology exam for patients at risk of ototoxicity.
CF Pulmonary Exacerbation

- CF Pulmonary Exacerbation: episode of acute or subacute worsening of respiratory symptoms from patient’s baseline
- Criteria that help define and exacerbation:
  - Decrease in FEV1 of > 10% from baseline
  - Increase cough
  - Increased/change in sputum
  - Increase rate or work of breathing
  - New findings of chest exam
  - Decreased exercise tolerance
  - Decrease in SpO2 >10% from baseline
  - New findings on chest radiograph
  - Weight loss of >5% of body weight
  - Fever, >38°C >4 hours in a 24 hour period, > 1 time in last week
  - School/work absenteeism in last week
- Quality of life is adversely affected with a decline in lung function with some patients not returning to a previous baseline
- Optimal treatment methods and standardization of those methods is important for improving quality of care and outcomes
- Optimal duration of therapy is not clear; the current standard is 10-14 days or until there is a plateau in lung function or clinical improvement (Flume 2009).

Intravenous Access

- Discuss type of IV access with admitting attending or attending of service
- Peripherally inserted central catheter (PICC) is preferred over peripheral IVs based on longer lifespan of line, patient satisfaction, and lower rate of complications, specifically including CLABSI and bacteremia.
- Many CF patients require PICC placement by IR due to prior thrombus, difficult access, need for sedation, etc.
- Antibiotics should be started promptly and not delayed significantly for PICC access. A peripheral IV should be placed if needed to prevent delay in treatment.

CF Annual Labs

- CBC with differential
- BMP
- LFT, GGT
- PT, PTT
- Vitamin A, Vitamin E, 25-OH Vitamin D
- IgE
- HbA1C – if indicated
- ESR
- Urine analysis
- Urine pregnancy test if indicated
**CF-related Diabetes Screen**

- Patients with CF are at risk of developing diabetes due to insulin deficiency from loss of pancreatic cell endocrine function over time. There may also be a component of insulin resistance especially during times of illness, stress or treatment with glucocorticoids.
- This risk increases in children 10 years old and older
- Hyperglycemia may worsen during an acute illness or with glucocorticoid treatment
- Hemoglobin A1C is not recommended for CF-related diabetes screening
- CF-related Diabetes screening (age 10 years and older)
  - Point of care glucose: daily A.M. fasting and once daily 2-hour post-prandial levels for 2 days.
  - If receiving supplemental tube feeding: replace AM fasting glucose with glucose check at middle and end of feeds for 2 nights.
  - If fasting glucose ≥ 126 mg/dl or any post-prandial ≥ 200 mg/dl continue monitoring for total of 72 hours.
    - If levels remain elevated, consult endocrine.

**Antibiotics**

- Intravenous antibiotics are used to treat the airway infection in a CF exacerbation. Occasionally, oral antibiotics are also used.
- Typically antibiotics are selected to which pathogens are susceptible, but in chronic CF airway infection, it may be impossible to choose antibiotics to which all identifiable pathogens are susceptible (Flume 2009).
- Currently, antibiotics are selected based on prior respiratory cultures, minimizing toxicity, drug resistance, and patient history of tolerance and improvement.
- The standard approach to antibiotic treatment of *Pseudomonas aeruginosa* (or suspected/presumed Pseudomonal infection) is to use two antibiotics, typically one beta-lactam and one aminoglycoside (Flume 2009).
- Follow CF specific dosing regimens.

**Tobramycin Dosing and Monitoring**

- Once daily dosing is preferred for patients with CF
  - This is based on improved concentration-dependent killing of bacterial and decreased risk for toxicity (Flume 2009).
- Dosing and monitoring
  - With once daily dosing, a trough is to be drawn prior to second dose with goal of <2 mcg/ml
  - With traditional three times per day dosing a trough is to be drawn 30 minutes prior to the 4th dose and a peak 30 minutes after the 3rd dose. Goal ranges for trough is <2 mcg/ml and for peak is 5-10 mcg/ml.
  - Do not draw drug levels from a line
  - Repeat weekly peak, trough and creatinine while on therapy if indicated.

**Completion of Therapy at Home**

- Assessment for home IV's – some patients can complete therapy at home. This should be discussed on every patient at the beginning of admission and assessed throughout the admission
- Criteria for possible transition to home for completion of IV antibiotics (Patient must meet all criteria and assessed as safe for continued therapy at home. The home setting should provide support and resources equivalent to the hospital setting)
  - Prior clinical response to inpatient intravenous antibiotic treatment and demonstrated tolerance of antibiotics
  - Stable intravenous access
  - Medically sophisticated caretakers at home who understand how to administer medications and can assess for side effects and complications of therapy
  - Stable social support services
  - Access to interval clinical assessment, including pulmonary function testing
  - No new onset of CF related complications
  - Ability to continue aggressive plan of care
  - No additional comorbidities that complicate care
  - Level of fatigue not significant enough to limit ability to do therapies
  - Ability to maintain enteral or oral fluids
  - Established therapeutic level of tobramycin
  - Safe plan for transport to home.

**Spirometry**
- Spirometry is done in patients 5 years and older to assess for improvement in lung function and response to therapy

**Antimicrobial Cheat Sheet**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
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</thead>
<tbody>
<tr>
<td>Zosyn (Piperacillin/Tazobactam)</td>
<td>100 mg/kg/dose IV Q8h (max 4g Piperacillin)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>50 mg/kg/dose IV Q8h (max 2g/dose)</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&gt;5 years old 10 mg/kg/dose IV Q24h</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&lt; 5 years old 3.3 mg/kg/dose IV Q8h</td>
</tr>
<tr>
<td>Monitoring: Trough</td>
<td>prior to second dose – level &lt;0.3 mcg/mL</td>
</tr>
<tr>
<td>Amikacin</td>
<td>10 mg/kg/dose IV Q8h</td>
</tr>
<tr>
<td></td>
<td>Monitor peak and trough at 3rd dose; Peak 20-25 mcg/mL; Trough 5-8 mcg/mL</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>30 mg/kg/dose IV Q24h</td>
</tr>
<tr>
<td></td>
<td>Monitor Trough prior to 2nd dose; level &lt;5 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>30 mg/kg/day IV Q8-12h (max 1.2g/day)</td>
</tr>
<tr>
<td></td>
<td>40 mg/kg/day PO Q12h (max 2g/day – typical 750 PO Q12h for adult)</td>
</tr>
</tbody>
</table>

*most commonly used regimen is Zosyn or Ceftazidime + aminoglycocide (Tobramycin)*

**Anti-staphylococcal**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bactrim (Sulfamethoxazole and Trimethoprim)</td>
<td>8-12 mg TMP/kg/day PO Q12h (max: 160 mg TMP/dose)</td>
</tr>
<tr>
<td>Adult</td>
<td>1-2 DS tabs PO Q12h</td>
</tr>
</tbody>
</table>
**Doxycycline**

> 8 years: 2-4 mg/kg/day PO Q12h (max 200 mg/day)

**Vancomycin**

15 mg/kg/dose IV Q6h

- Monitor trough prior 4th dose – level 15-20 mg/mL
- Adult (>46 kg): 15 mg/kg/dose IV Q12h
- Monitor trough prior 4th dose – level 15-20 mg/mL

**Inhaled Antibiotics (usually reserved for non-exacerbation admissions or when having renal compromise with aminoglycosides)**

- **TOBI (Tobramycin)**: 300 mg inhaled Q12h
- **TOBI Podhaler**: 112 mg (4 x 28 mg capsules) every 12 hours
- **Cayston (Aztreonam)**: 75 mg inhaled Q8h
- **Colistin**: 75-150 mg in 3 mL of NS (4 mL total) inhaled Q12h

**Antifungal**

- **Sporanox (Itraconazole)**
  - Child: 5-10 mg/kg/day divided Q12h (max 400 mg/day)
  - Adult: 200 mg PO Q12h (for ABPA)

- **Voriconazole**
  - < 12 years: 9 mg/kg/dose PO every 12 hours (max 350 mg/dose)
  - > 12+ < 40 kg: 100 mg PO Q12h (max 300 mg/day)
  - > 12+ > 40 kg: 200 mg PO Q12h (max 600 mg/day)

**Other**

- **Azithromycin**
  - 18-35.9 kg: 250 mg PO QM/W/F
  - > 36 kg: 500 mg PO QM/W/F

**Requires Infectious Disease involvement**

- **Cefepime**: 50 mg/kg/dose IV Q6-Q8h (max 2g)
- **Meropenem**: 40 mg/kg/dose IV Q8h (max 2g)
- **Zyvox (Linezolid)**
  - < 12 years: 10 mg/kg/dose PO Q8h (max 600 mg/dose)
  - > 12 years: 600 mg PO Q12h
- **Tigecycline**: 1.2 mg/kg/dose IV Q12h (max 50 mg)
- **Posaconazole**: (less side effects than Voriconazole)