Cystic Fibrosis: Pulmonary Exacerbation v2.3

Approval & Citation | Summary of Version Changes | Explanation of Evidence Ratings

ADMISSION AND TREATMENT
Use Pulmonary CF Admit Plan

Inclusion Criteria
Age ≥ 1 year with cystic fibrosis admitted for pulmonary exacerbation

Exclusion Criteria
- ICU Admission
- Newborn with meconium ileus
- Admission for initiation of insulin therapy without pulmonary exacerbation
- Primary reason for admission is eradication of Pseudomonas, bowel obstruction, appendicitis, other acute GI condition, or acute bronchiolitis
  (Per attending MD discretion, use CF Admit Plan and check "exclude from" pathway)

Admit Criteria
Meets several Fuchs criteria:
- Decrease FEV1 of > 10% from baseline
- Increased cough
- Increased/change in sputum
- Fever, > 38˚C > 4 hrs in 24 period, > 1 time in last week
- Weight loss > 5% of body weight
- School/work absenteeism in last week
- Increased rate or work of breathing
- New finding on chest exam
- Decreased exercise tolerance
- Decrease in SaO2 > 10% from baseline
- New finding(s) on chest x-ray

Plan IV Access
- Determine type of IV access
- Consult vascular access team on admission if PICC indicated
- PIV if PICC placement unavailable within 6 hours
- If prior history of line-related thrombus, consider prophylactic anticoagulation

Initiate Therapy
(using Pulmonary Cystic Fibrosis Plan)

Health Status Assessment
- Height (length), weight at admit and every other day, BMI, Vitals, Oximetry
- Spirometry ≥ 5 years of age on admit if not done in clinic then twice a week
- Routine respiratory assessment (cough, WOB, sputum quantity and color)

Lab
- Check results of last CF Respiratory Culture
- If not done within last 28 days, send CF Respiratory Culture (sputum if expectorating, oropharyngeal (OP) culture if unable to expectorate) to CF microlab
- If OP culture needed, call CF nurse
- In expectorating patient, send sputum for AFB stain and culture if not done in the last year or if clinically indicated
- BUN/serum creatinine on admission, then serum creatinine every 3 days
- Monitor for antibiotic toxicity by checking antibiotic specific baseline and weekly labs
- Annual labs (use CF Annual Lab Orderset)
- CF related diabetes screening for patients ≥ 10 years of age
  - If any fasting ≥ 126mg/dl or any post-prandial ≥ 200mg/dl, send next glucose level as serum level, and continue to monitor for total of 72 hours
  - If levels remain elevated, consult endocrinology
- **Airway Clearance Protocol**
  - Four times/day (modality based largely on age, patient preference/adherence, safety, and RT assessment), first treatment by 10am

Nutrition
- CF diet, supplement if indicated (enteral or PO)
- 3 meals, 3 snacks per day, first meal by 9am

Nursing
- Modified activity plan
- Contact isolation, at minimum
- Give patient and family Going to the Hospital for a CF Lung Exacerbation (PE912)

Medication
- CFTR modulators
  - Patient supplied CFTR modulators are preferred
  - Home maintenance medications
- Antibiotics
  - Choice based on respiratory culture sensitivities and patient history of tolerance or improvement
  - If treating with tobramycin, draw level 2 and 6 hours after 2nd dose for pharmacy to calculate AUC
  - Do not draw antibiotic levels from line
- Steroids if indicated
- If volume depleted, bolus until euvolemic, then maintenance

Consults
- CF Nutritionist, CF Social Work, Child Life, Physical Therapy
- Endocrinology for patient with CF related diabetes
- Otolaryngology as needed

All disciplines
- Begin CF education

! May need to modify airway clearance for hemoptysis, chest tube or pneumothorax

Go to Inpatient

! Review drug-drug interactions with pharmacist (high-dose ibuprofen and CFTR modulators)

Last Updated: March 2024
Next Expected Review: May 2021

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INPATIENT

Therapy or Assessment

Elevated Glucose

- If any fasting ≥ 126mg/dl or any post-prandial ≥ 200mg/dl, send next glucose level as serum level, and continue to monitor for additional 72 hours
- If levels remain elevated, consult endocrinology

Adjust treatment plan if no improvement
(The following options may be considered)

- Adequacy of airway clearance
- Consider other pathogens (repeat sputum culture, obtain AFB culture for non-tuberculous mycobacterium)
- Consider imaging
- Screen for ABPA
- Consider steroid burst
- Adjust antibiotics
- New baseline

!
If antibiotics continue beyond 14 days check safety labs (and tobramycin recheck AUC)

Criteria for Possible Transition to Home for Completion of IV Antibiotics

- Prior clinical response to inpatient intravenous antibiotic treatment and demonstrated tolerance of antibiotics
- Therapeutic antibiotic levels
- Stable intravenous access
- Medically sophisticated caretakers at home
- Stable social support services
- Access to interval clinical assessment, including Pulmonary Function Testing
- No new onset of CF 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
- Able to take maintenance enteral or oral fluids
- Established therapeutic level of tobramycin
- Safe plan for transport home
- Access the ability to perform laboratory monitoring

Patient candidate for home abx?

- No → **Complete Inpatient therapy**
- Patient needs continued antibiotics and meets criteria to go home →

Prepare for Home IV Antibiotics

- Set up home IV teaching
- Arrange home care
- Arrange spirometry
- Arrange and order outpatient labs

Is patient plateaued near baseline?

- No → back to Therapy or Assessment
- Yes →

Maintenance Medications and Care Coordination

- Ensure patients are prescribed all appropriate maintenance medications at the proper dosage and have access to specialty medications.
  - Medication reconciliation is complete
  - Update with current status and plan of care
    - Patient/family
    - All community care providers
- Follow-up appointments are scheduled
  - **No home IV:** CF Clinic visit for 4-6 weeks after therapy is completed
  - **Home IV antibiotics**: CF Clinic visit and / or PFTs on day 7-14 of therapy
  - Consult service follow-up as requested
  - Annual audiology exam for patients at risk for ototoxicity
  - Annual oral glucose tolerance test (OGTT) for patient 10 years and older

Discharge Criteria

- Patient's clinical signs and symptoms of pulmonary exacerbation and other co-morbidities have resolved or returned to baseline
- Pulmonary function tests have improved and plateaued or returned to prior baseline
- Care coordination needs of patient and family for equipment or education for transition home are met

Yes →

Discharge Instructions

- Discharge medications
- New Therapies (*for SCH only*)
- Cleaning (*for SCH only*)

For questions concerning this pathway, contact: CysticFibrosisPathway@seattlechildrens.org

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Components of Inpatient Treatment

- Provider to order airway clearance protocol
  - Patient education
  - Assessment of best modality by RT
  - Airway clearance scheduled four times daily
- Monitoring for medication associated toxicities
  - Antibiotics, NSAIDs, antifungals, antivirals, etc and ETI
- Psychosocial support
- Team approach is important

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Return to Admission Return to Inpatient

Recent Changes and Important Highlighted Aspects of Care

Improve quality and safety of care for children with cystic fibrosis (CF) by developing a standardized algorithm and conversion to powerplan for treatment of CF pulmonary exacerbation.

Evaluation at the time of admission emphasizes both assessing the patient's exacerbation and reviewing the patient's current heath status.

- Obtain respiratory culture if not done the past 28 days.
- If not obtained in the past 9 months, annual CF laboratory panel will be obtained to help minimize number of venipunctures.
- Assessment of intravascular volume status to determine need for additional IV fluids to minimize risk for nephrotoxicity.
- Screening for CF-related diabetes for patients 10 and older will occur based on the 2010 national guidelines for CF-related diabetes screening during pulmonary exacerbation.
- Endocrinology consultation on admission for patients with CFRD on insulin therapy
- Endocrinology consultation for patients with positive screening tests.
- Continued use of peripherally inserted central catheter (PICC) is recommended for delivery of IV antibiotics.
- Once daily tobramycin dosing continues to be recommended as the standard of care.
- Appropriate antibiotic specific laboratory monitoring for toxicity is recommended.
- Increased monitoring for Acute Kidney Injury (AKI) for those on nephrotoxic medications.
- Inclusion of RT assessment pathway to optimize airway clearance, and tracking of frequency of airway clearance.
- Discharge Care Coordination should be initiated early for all patients:
  - those who will transition to home on IV antibiotics
  - those who stay for duration of treatment.

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Admit and Initiate Therapy

Continue prescribed home medications with following exceptions:

1. Patients prescribed CFTR modulators should continue during admission. Using patient's own supply during hospital admission is the preferred option. If unable to obtain patient own supply, pharmacy will have specific CFTR modulator options available.
2. May need to restart Dornase Apha or hypertonic saline
3. Discontinue high-dose NSAID while on nephrotoxic drugs
4. Review home antibiotics with the CF team (there is insufficient evidence to recommend for or against the continuation of inhaled antibiotics during treatment of exacerbation).

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CFTR Modulators

CFTR modulators

- Trikafta® (elexacaftor/tezacaftor/ivacaftor)
- Kalydeco® (ivacaftor)
- Orkambi® (lumacaftor/ivacaftor)
- Symdeko® (tezacaftor/ivacaftor)

Patients and/or families are requested to bring 2-week supply upon admission and follow the Non-formulary and Patient Supplied Medication policy, 11123 (*for SCH only*)

Identify at admission if patient is unable to supply their own CFTR modulator, discuss with pharmacy about what options are currently stocked and available

Pharmacy may not have an alterative available, requests to obtain non formulary dosage forms will need approval from P&T committee and may take 1-4 days to obtain.

- Example- Trikafta 80/40/60 & 59.5 granules are non formulary and there is no formulary option. If not provided by family, escalate to pharmacy as soon as possible to seek approval to purchase and obtain. This may take upwards of 4 days in some situations.

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CF Pulmonary Exacerbation

- **CF Pulmonary exacerbation**—episode of acute or sub-acute worsening of respiratory symptoms from patient's baseline
- Several criteria define an exacerbation:

- Decrease FEV1 of >10% from baseline
- Increased cough
- Increased/change in sputum
- Fever, >38°C >4 hrs in 24 hr period, >1 time in last week
- Weight loss >5% of body weight
- School/work absenteeism in last week
- Increased rate or work of breathing
- New finding on chest exam
- Decreased exercise tolerance
- Decrease in SaO2 >10% from baseline
- New finding(s) on Chest X-ray

- There is an adverse impact on quality of life and often an adverse impact on lung function decline with some patients not returning to previous baseline (Sanders, 2010, 2011)
- Optimal treatment methods and standardization of those methods is important for improving quality of care and outcomes
- Although the optimal duration of treatment is not clear, the current standard of care is to treat for 10-14 days or until there is a plateau in lung function or clinical improvement. [LOE: E (Expert Opinion)] (Guideline of care 1997, Flume 2009)

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Return to Admission Return to Inpatient

Admit and Initiate Therapy (Phase 1)

- Discuss type of IV access with the admitting attending
- Continued use of peripherally inserted central catheter (PICC) is preferred over peripheral IVs based on benefits of longer lifespan of the line, patient satisfaction, and based on the available literature showing a low rate of complication. [LOE:✪✪○○, (Prayle, 2010), (Bui, 2009), (Tolomeo, 2003)]
- Many CF patients require PICC line placement by interventional radiology (IR) due to prior thrombus, difficult access, need for sedation, etc.
- Antibiotics should be started promptly. Therefore, peripheral IV will be placed if needed to prevent delay of treatment.

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Screening and Monitoring for Cystic Fibrosis Related Diabetes

- Patients with CF are at risk for developing diabetes mainly due to insulin deficiency from loss of pancreatic endocrine function over time. There may also be a component of insulin resistance during times of illness, stress, or with glucocorticoid treatment.
- The risk of diabetes increases in children 10 years of age and older.
- Hyperglycemia may worsen during illness (such as pulmonary exacerbation) or with glucocorticoid treatment.
- The following recommendations for inpatient diabetes screening and monitoring are based on a national guideline developed by evidence based review of the literature and expert consensus.[LOE: ✪✪○○, (Moran, 2010)]
- Hemoglobin A1C is not recommended for CF related diabetes screening [LOE: ✪✪✪✪, (Moran, 2010)]

CF related diabetes screening for patients ≥10 years of age

- If any fasting ≥126mg/dl or any post-prandial ≥200mg/dl, send next glucose level as serum level, and continue to monitor for total of 72 hours
- If levels remain elevated, consult endocrinology

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Admit and Initiate Therapy (Phase 1)

Antibiotics

- Intravenous antibiotics are used to treat the airway infection in CF. Occasionally, oral antibiotics are also prescribed.
- Clinicians typically select antibiotics to which the pathogens are susceptible, but in chronic CF airway infections, it may be impossible to select antibiotics to which all identified pathogens are susceptible. (Flume 2009)
- Currently, antibiotic selection is based on prior respiratory cultures, minimizing toxicity, drug resistance, and patient history of tolerance/improvement.
- The standard approach to antibiotic treatment of Pseudomonas aeruginosa (one of the most common CF pathogens) is to use two antibiotics, typically one beta-lactam and one aminoglycoside. (Flume 2009 [LOE: E], Gibson 2003)

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Tobramycin Dosing and Monitoring

Tobramycin is one of the most commonly used antibiotics for CF pulmonary exacerbation

- Once daily dosing is preferred for CF patients
  - This is based on improved concentration dependent killing of bacteria and a decreased risk for toxicity
  - This has been established by previous literature (see evidence table in CF pulmonary exacerbation guidelines, Flume 2009) [LOE: E], (Smyth 2006)
- Dosing and monitoring is in Seattle Children's formulary
  - Draw level 2 and 6 hours after 2nd dose for calculation of AUC
  - Do not draw drug levels from a line
  - Monitor serum creatinine weekly (renal function monitoring frequency may need to be modified if patient is on multiple nephrotoxic drugs)
  - Repeat AUC and creatinine if > 14 days of therapy

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Return to Admission Return to Inpatient

Approval and Citation

Approved by the CSW Cystic Fibrosis team for May 4, 2016 go-live

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Retrieval Website: http://www.seattlechildrens.org/pdf/cystic-fibrosis-org-pathway.pdf

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Summary of Version Changes

- **Version 1.0 (12/19/2011):** Go live
- **Version 1.2 (9/17/2012):** Added bronchiolitis to inclusion criteria, clarified glucose testing for patients on nightly enteral feeds
- **Version 1.3 (10/9/2012):** Added age 1 year and older to inclusion criteria
- **Version 2.0 (5/4/2016):** Added renal toxicity screening
- **Version 2.1 (9/14/2017):** Updated email contact
- **Version 2.2 (10/9/2017):** Updated citation
- **Version 2.3 (3/19/2024):** Added information about using patient's home supply of CFTR modulators while inpatient

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Evidence Ratings

We used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial, or observational studies. The rating is then adjusted in the following manner:

Quality ratings are *downgraded* if studies:

- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings can be *upgraded* if it is felt that:

- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Quality of Evidence:

✪✪✪✪ High quality
✪✪✪○ Moderate quality
✪✪○○ Low quality
✪○○○ Very low quality
Expert Opinion (E)

Reference: Guyatt G et al. J Clin Epi 2011: 383-394

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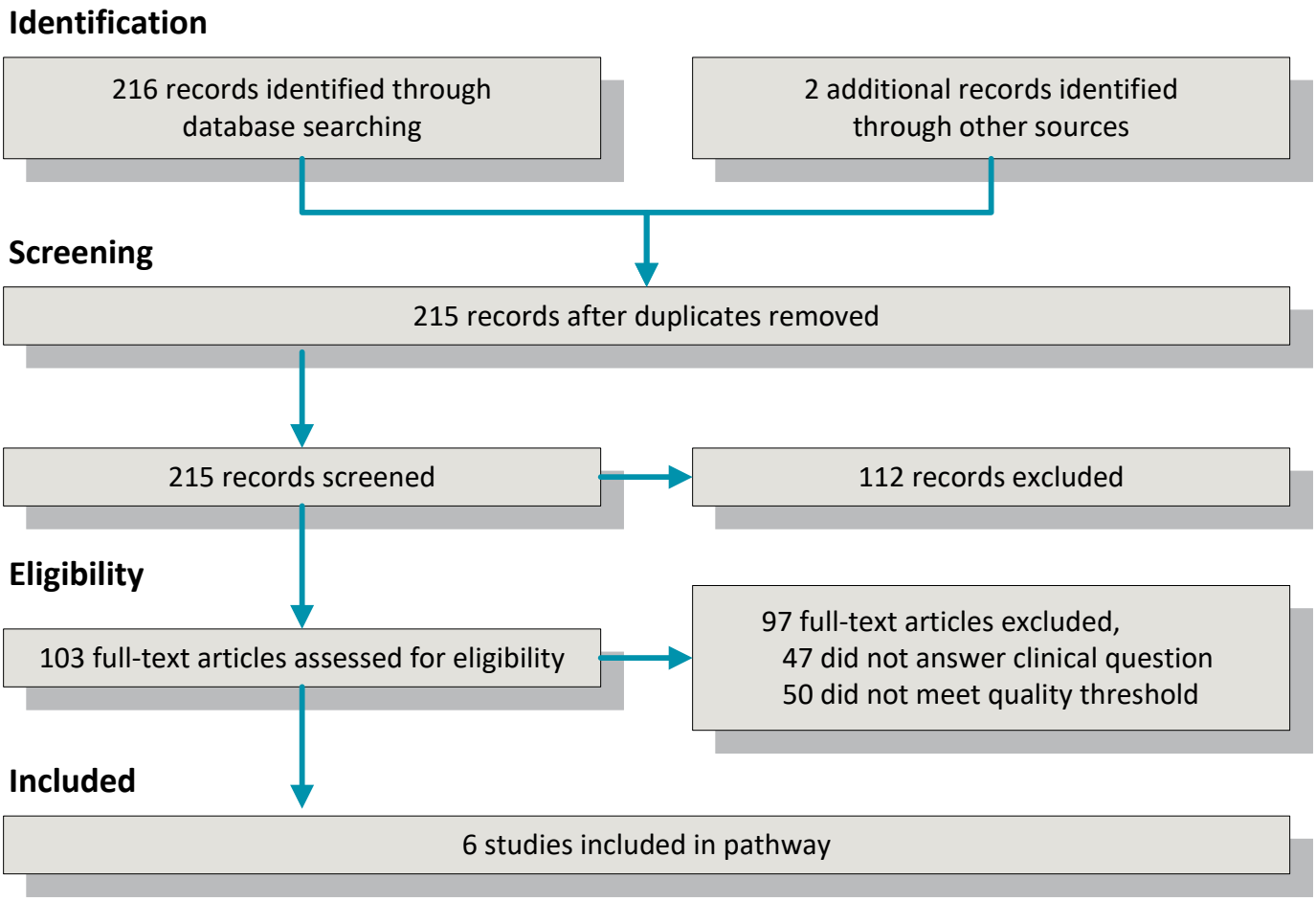
Bibliography

Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian, Susan Klawansky. Searches were performed on July 7 and 8, 2011 in the following databases: on the Ovid platform – Medline (2000 to date), Cochrane Database of Systematic Reviews (2005 – June 2011), Cochrane Central Register of Controlled Trials (2000 – 2nd quarter, 2011); elsewhere – CINAHL (2000 to date), Clinical Evidence, DynaMed and TRIP. Retrieval was limited to English language but no age limits were imposed. In Medline, appropriate Medical Subject Headings (MeSH) were used, along with text words, and the search strategy was adapted for other databases using their controlled vocabularies, where available, along with text words. Concepts searched were cystic fibrosis and either the use of PICCs or issues related to diabetes/hyperglycemia/blood glucose. Per the project team members, only the first question relating to cystic fibrosis and PICCs was searched in CINAHL.



Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

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Medical Disclaimer

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

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