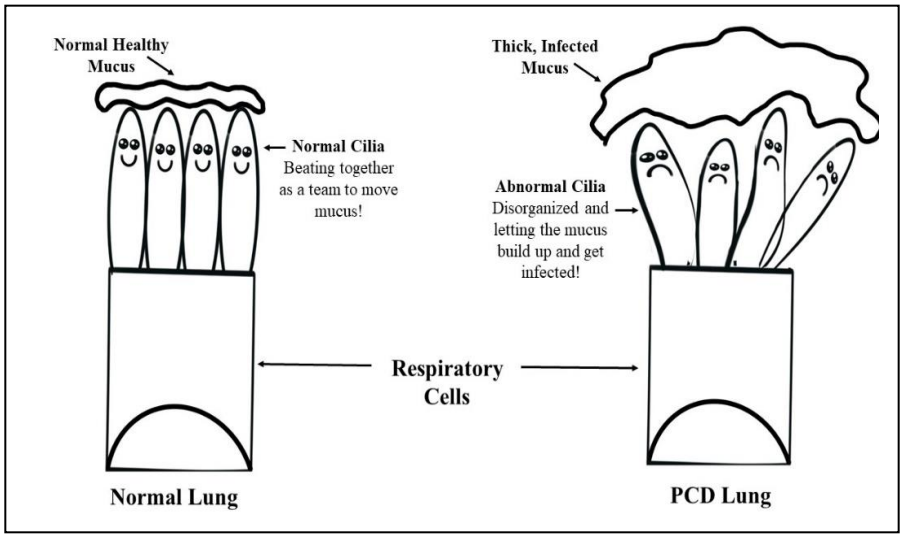
Primary Ciliary Dyskinesia (PCD) Cheat Sheet

What is PCD?

PCD is a rare lung disease that is caused by a variety of genetic mutations affecting more than 45 genes. The genetic mutation results in a structural defect in cilia. This defect impairs the function of motile cilia in the respiratory epithelium (nose and lung) which leads to impaired mucociliary clearance. Without the cilia moving the mucus along the respiratory tract, the mucus stagnates, thickens and because a prime breeding ground for infections (both bacterial and fungal).



Because motile cilia are key players in organ development in the fetus as well as in other parts of the body, there are several other key organ systems that may be affected. Abnormal positioning of any organ (i.e. heart on right side of chest instead of the left) is highly indicative of a ciliary defect. And patients with PCD can have abnormalities of their eyes, cerebrospinal fluid management (hydrocephalus) as well as their reproductive tracts due to dysfunction of cilia in those areas.

How rare is PCD?

PCD is rare-affecting 1:15,000 individuals. However, as symptoms of PCD are common, we estimate that up to 10% of patients with PCD are not diagnosed and just reassured about their chronic respiratory symptoms. In fact, most people with PCD see a physician more than 50 times before getting a PCD diagnosis. The average age at diagnosis is 5.3 years.

What are the symptoms of PCD?

Patients with PCD typically meet at least 2 of 3 clinical diagnostic criteria:

- 1-chronic, year round, daily cough from infancy (~100%),
- 2-chronic, year round daily nasal congestion OR chronic sinusitis (~80%)
- 3-Organ laterality defects (organs positioned abnormally).

About 80% of patients also have recurrent otitis media but this is insufficient to meet diagnostic criteria for further testing. Patients may also have respiratory distress as a

newborn which is a fourth diagnostic criteria-less commonly remembered by patients and parents.

How is PCD diagnosed?

First a diagnosis of Cystic Fibrosis must be excluded by obtaining a negative sweat test. Patients must meet 2 of the 3 diagnostic criteria to pursue further testing for PCD. If nasal NO is available, this is the preferred initial test. If nasal NO is low, the measure is repeated to confirm the positive test result. Then further genetic testing is perform. In rare cases, where we cannot diagnose with genetics and nasal nitric oxide, a ciliary biopsy in the nose may be performed. Our biopsies are sent to the Mayo Clinic in accordance with PCD Foundation guidelines.

If nasal NO is not available or the subject is unable to perform nasal NO testing, an extended genetic panel is ordered. At the New England Primary Ciliary Dyskinesia Center, for all genetic testing, we place a referral to a medical geneticist who provides pre/post test counseling as well as interpretation of the results in concert with our adult and pediatric clinical teams. Currently, as preferred by the PCD Foundation, we order testing through Invitae Genetics (Invitae Primary Ciliary Dyskinesia Panel).

What type of care do people with PCD need?

People with PCD should be managed by a team with expertise in PCD. This team is typically overseen by a pulmonologist with expertise in PCD. During childhood, people with PCD should been seen by an otolaryngologist at least once a year to have their nasal passages evaluated with an in office nasal endoscopy. As people age, they may see the otolaryngologist as needed. Careful attention to maintenance of normal hearing is key at any age.

Because PCD can cause organ position abnormalities in the cardiac, GI and renal systems as well as affect the reproductive systems, the multidisciplinary team will handle evaluation and referral as needed. Other key team members include respiratory therapists, nurses, social workers and nutritionists. The goal of the team is to address the physical and mental health needs of people with PCD.

Below is a general summary of the daily and surveillance therapies for people with PCD[1]:

TABLE 8—Suggested Schedule of Investigations and Clinical Care in Primary Ciliary Dyskinesia

Clinical visits
- Pulmonology: 2–4 times/year
- Otolaryngology: 1-2 time/year in children, as needed in adults
- Audiology: at diagnosis and as needed per otolaryngology
- Reproductive medicine: As clinically needed

Long-term surveillance
- Chest radiography: every 2–4 years
- Chest computed tomography: consider at least once after 5–7 years old (when sedation not required and images are of highest quality)[1]
- Airway microbiology cultures: 2–4 times/year
- Non-tuberculosis mycobacterial cultures: every 2 years (and with unexplained clinical decline)
- Pulmonary function testing: 2–4 times/year
- ABPA testing: IgE levels ± evidence of aspergillus specificity at diagnosis, with new onset wheezing, unexplained clinical decline

Preventative therapies
- Airway clearance: daily
- Nasal sinus lavage: daily (when pertinent)
- Standard vaccinations: per local schedule
- Influenza vaccine: annually[2]
- 13-valent pneumococcal vaccine: per ACIP guidelines[3]
- 23-valent pneumococcal vaccine: per ACIP guidelines[4]
- RSV immunoprophylaxis: consider monthly in first winter[5]

[1]And as clinically indicated on a case by case basis.
[2]After 6 months old, including household members.
[3]ACIP guidelines.
[4]ACIP guidelines.
[5]Specifically consider in infants with complicated respiratory courses, including prematurity, prolonged mechanical ventilation, prolonged need for supplemental oxygen, need for home supplemental oxygen, or frequent respiratory illnesses.

In addition to the above, in accordance with guidelines, our patients will receive an in-person airway clearance educational session annually as well as one by telehealth in their homes. Patients will be monitored for appropriate nutrition to maintain growth, good protein intake and normal vitamin D levels[2].

What type of therapies are common with PCD?

People with PCD should be doing airway clearance therapy every day. Modalities should be selected based on the age and cognitive/manual dexterity levels of the patient[3]. See table at the right. Our least preferred therapy is the vest as it doesn't intrinsically have positive end expiratory pressure and doesn't inspire patient effort. If vest is used, significant education regarding huff coughing and positioning will be performed.

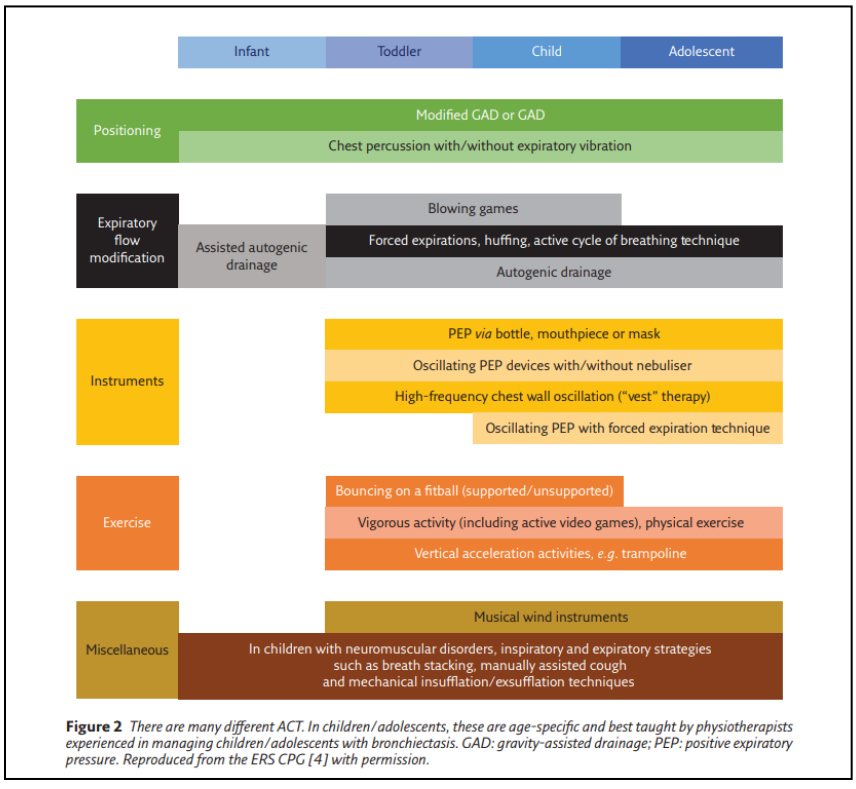


Figure 2 *There are many different ACT. In children/adolescents, these are age-specific and best taught by physiotherapists experienced in managing children/adolescents with bronchiectasis. GAD: gravity-assisted drainage; PEP: positive expiratory pressure. Reproduced from the ERS CPG [4] with permission.*

Currently, we believe oral azithromycin MWF is beneficial for patients with PCD to diminish the amount of pulmonary

exacerbations. Patients should be aggressively treated for bacterial infections and eradication of Pseudomonas aeruginosa should be performed. Those patients with chronic Pseudomonas aeruginosa colonization usually require maintenance inhaled antibiotics (eg. TOBI/Cayston 28 days on/28 days off or continuously.

Patients may be prescribed other medications such as hypertonic saline to assist with clearance of secretions. Routine prescribing of dornase alpha (may be harmful), other oral antibiotics, inhaled corticosteroids (without asthma diagnosis) are NOT recommended[4].

The New England Primary Ciliary Dyskinesia Center Team

Connecticut Children's (0-18 years)

- **Center Director:** Melanie Sue Collins, MD
- **PCD MDs:** Craig Lapin, MD, and Jamie Harris, MD
- **PCD Coordinator:** Ashley Barber, RN
- **Respiratory:** Lynn Dougherty, RRT, and Stacey, Hallgren, RRT
- **Nutritionist:** Lisa Devine, RD
- **Otolaryngology:** Christopher Grindle, MD

UCONN Health (>18 years)

- **Center Director:** Mark L. Metersky, MD
- **Coordinator:** Joanna Wroblewski, FNP-BC
- **Otolaryngology:** Todd E. Falcone, MD
- **Genetics:** Jaclyn M. Beirne, MD

References

1-Shapiro AJ, Zariwala MA, Ferkol T, Davis SD, Sagel SD, Dell SD, Rosenfeld M, Olivier KN, Milla C, Daniel SJ, Kimple AJ, Manion M, Knowles MR, Leigh MW; Genetic Disorders of Mucociliary Clearance Consortium. Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review. Pediatr Pulmonol. 2016 Feb;51(2):115-32. doi: 10.1002/ppul.23304. Epub 2015 Sep 29. PMID: 26418604; PMCID: PMC4912005.

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