



Airway Clearance Indications: Genetic Disorders of Mucociliary Clearance

Primary Ciliary Dyskinesia (PCD) (aka Kartagener Syndrome; Immotile Cilia Syndrome)

Primary ciliary dyskinesia is an umbrella term for genetic disorders of the structure and/or function of cilia. Cilia are microscopic projections arising from the wall of the airway that beat in a coordinated fashion to move debris-laden mucus up and out of the lungs. Primary ciliary dyskinesia is one of three recognized genetic disorders of mucociliary clearance, along with cystic fibrosis (CF) and pseudohypoadosteronism (PHA). As the classification implies, all three are characterized by profound disruption of the mucociliary clearance system, although the underlying pathophysiology and long term prognosis vary between them.

In primary ciliary dyskinesia, mutations in genes responsible for producing the proteins necessary to build and maintain a cilium result in global impairment in ciliary structure or function. This means that every body system that relies on ciliary activity will be affected, including the upper and lower respiratory tract, middle ears and reproductive organs (sperm tails in men and Fallopian tubes in women). Additionally, ciliary activity during embryonic development helps to determine organ placement so people with primary ciliary dyskinesia may exhibit unusual organ arrangements (*situs*) including *situs inversus* (complete mirror image reversal of chest and abdominal organs) or *situs ambiguus* (any organ arrangement that is not typical, but is not complete *situs inversus*--also called heterotaxy). Organ placement in primary ciliary dyskinesia is random. It is estimated that 6-18% of affected individuals will have *situs ambiguus*. Normal *situs* and *situs inversus* are split about evenly between remaining affected individuals. Kartagener syndrome is simply a name to identify primary ciliary dyskinesia with *situs inversus* and therefore is a subset of primary ciliary dyskinesia, not a separate disorder. In rare cases, ciliary activity in the ventricles of the brain may be impaired leading to hydrocephalus. There is increasing evidence of an association between congenital heart disease and primary ciliary dyskinesia, probably due to cilia-related disruptions in embryonic development of the cardiac system.

Primary ciliary dyskinesia is a recessive disorder, meaning both parents must carry a mutation for a child to have the disease. Cilia are complex structures and ciliary structure and function are regulated by many genes. Primary ciliary dyskinesia-causing mutations have been identified in several genes and researchers continue the search for all causative genetic mutations. Primary ciliary dyskinesia is a rare disorder, affecting approximately 1 in 12,000 – 16,000 individuals of all races, genders and ethnic origins. In isolated populations or cultures where intermarriage is common, the incidence can be much higher.

What Happens in Primary Ciliary Dyskinesia?

Effective mucociliary clearance requires mucus of the right amount and consistency working in a coordinated fashion with ciliary activity to keep airways clean and free of infection. In primary ciliary dyskinesia (formerly called 'immotile cilia syndrome') structural or functional defects of the cilia profoundly affect ciliary activity and disrupt the mucociliary clearance system. Because the disorder is genetic, symptoms are present at birth and newborn respiratory distress is a hallmark



of the disease. It is believed this occurs because ciliary activity is important in making the transition from the liquid environment of the womb to the gas (oxygen) environment after birth. Upper and lower respiratory infections begin almost immediately, leading to a vicious cycle of cycle of impaired mucociliary clearance, chronic infection and more damage to the airways. By early adulthood, most people with primary ciliary dyskinesia will have bronchiectasis. As the disease progresses quality of life declines and end-stage lung disease may lead to respiratory failure or the need for lung transplant.

How Airway Clearance Therapy Can Help in Primary Ciliary Dyskinesia

Because people with primary ciliary dyskinesia lack a functioning mucociliary clearance system, daily, lifelong airway clearance therapy is required. Keeping the airways clear of excess secretions and thereby reduce the incidence of inflammation and/or infection and is crucial to maintaining respiratory health. Airway clearance therapy using High Frequency Chest Wall Oscillation (HFCWO) has been demonstrated by clinical study to promote excess mucus clearance and improve bronchial drainage. Shear forces are created by HFCWO treatment that mechanically releases adhered secretions from the walls of the pulmonary tract. HFCWO has also been shown to reduce the viscosity of secretions which significantly improves mobilization of excess mucus. By replicating cough, HFCWO can effectively mobilize pulmonary secretions from smaller airways to larger airways where they can be coughed out, swallowed or suctioned.

Symptoms of Primary Ciliary Dyskinesia

- Neonatal (newborn) respiratory distress in term infant
- Lifelong history of chronic infections of lungs, sinuses and ears
- Chronic cough
- “Wheezing” or noisy chest
- Hearing loss
- Excessive drainage from nose and/or ears
- Situs abnormalities with history of upper and lower respiratory disease
- Congenital heart defects with history of upper and lower respiratory disease
- Retinitis pigmentosa or hydrocephalus with history of upper and lower respiratory disease
- Hemoptysis (blood in sputum)
- Bronchiolithiasis (lung “stones”)

For More Information on Primary Ciliary Dyskinesia:

1. Primary Ciliary Dyskinesia Foundation: www.pcdfoundation.org
2. GeneReviews overview of primary ciliary dyskinesia:
<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&partid=1122>
3. University of North Carolina, Chapel Hill PCD Research and Treatment Center:
<http://www.med.unc.edu/cystfib/PCD.htm>
4. eMedicine primary ciliary dyskinesia fact sheet: <http://www.emedicine.com/ped/topic1166.htm>