Centre universitaire de santé McGill

McGill University Health Centre

Montreal Chest Institute

A Rare Lung Disease //

A Short Guide to *Primary Ciliary Dyskinesia (PCD)*

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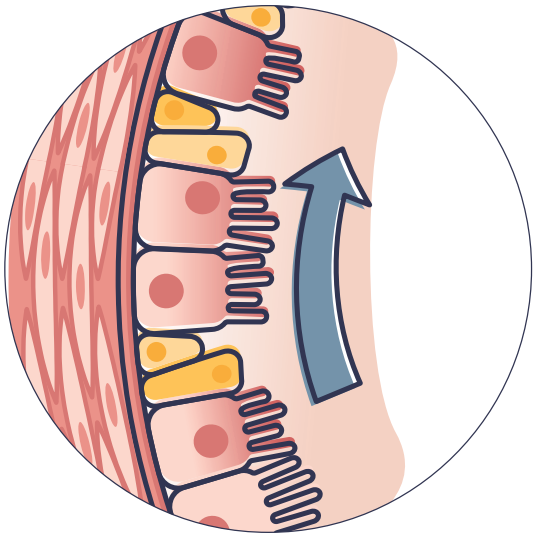
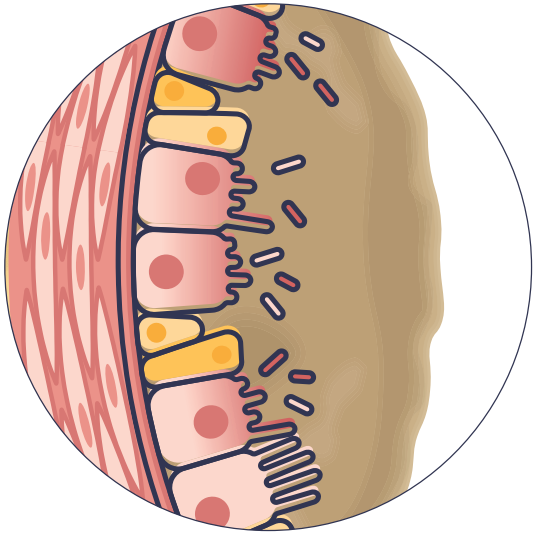
// What is Primary Ciliary Dyskinesia?

Primary Ciliary Dyskinesia (PCD) is a rare, inherited genetic disorder that affect the cells with moving cilia in the body. Cilia are tiny hairlike structures on the cells lining the respiratory tract and they play an important role in the nose, sinuses, ears and lungs, working to remove unwanted inhaled particles and germs that get stuck in your mucus.



NORMAL AIRWAY
- **Cilia intact**
- **Mucus swept up by cilia**

When the cilia aren't working properly, there is inadequate clearing of the mucus containing these inhaled germs and particles, resulting in frequent respiratory infections starting at a very early age. This may result in lifelong, progressive lung, sinus and ear diseases. PCD can also be associated with reversed or flipped organs (situs inversus), congenital heart diseases and fertility issues.

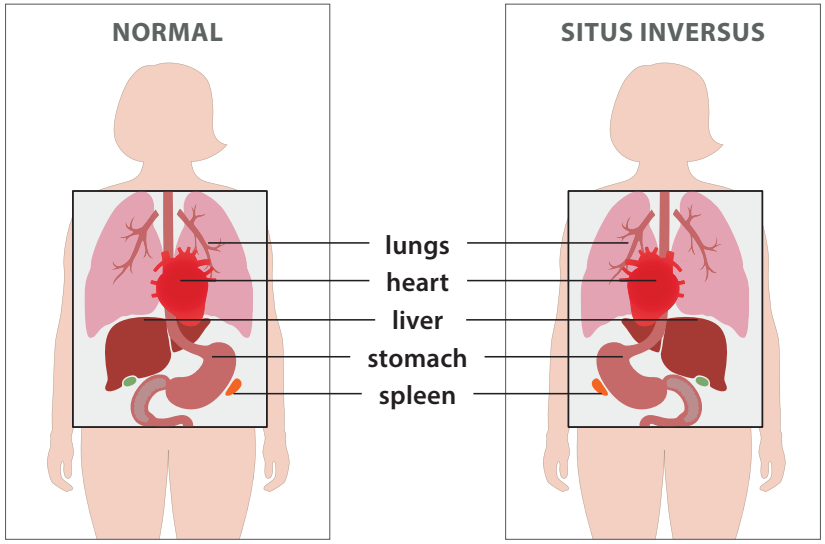


AIRWAY WITH PCD
- **Faulty cilia**
- **Mucus build up**

// What are the symptoms of PCD?

SITUS VARIATION

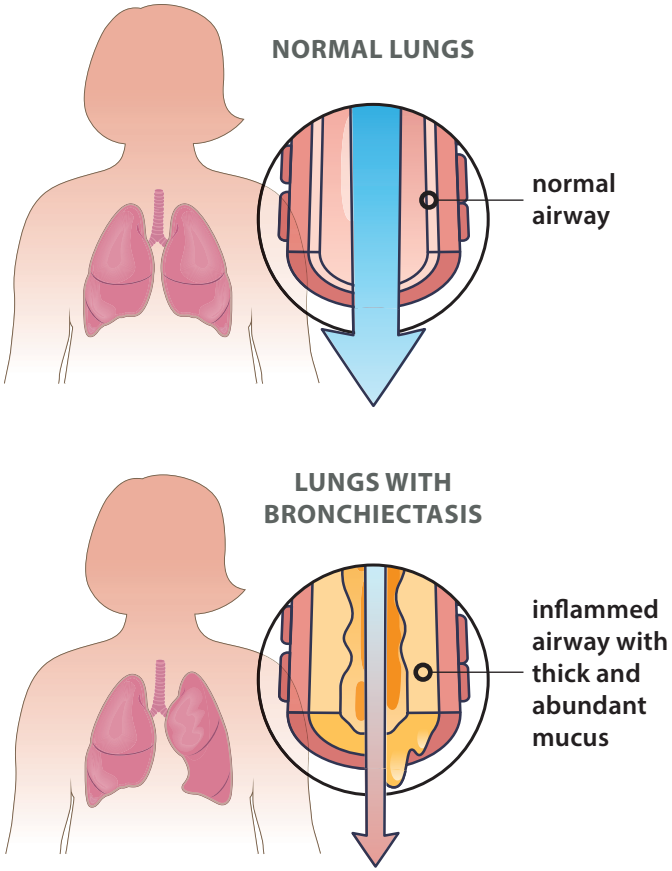
Situs Inversus Totalis, (mirror-image reversed organs from normal arrangement of heart on left, liver on right,etc.) appears in around 50% of PCD patients and can be detected on a routine chest x-ray.



PCD patients with *Situs Inversus Totalis* are sometimes labeled with the outdated term "Kartagener's syndrome." Less commonly, babies may be born with more complex organ arrangements, a condition known as *Situs Ambiguus* or "Heterotaxy", which often includes congenital heart disease. Most babies with PCD also have trouble breathing in the first days of life, often requiring days to weeks of extra oxygen and respiratory support in the neonatal intensive care unit. However, most cases of PCD are diagnosed later in life, and the trouble breathing after birth does not frequently trigger PCD investigations, unless babies also have situs inversus totalis.

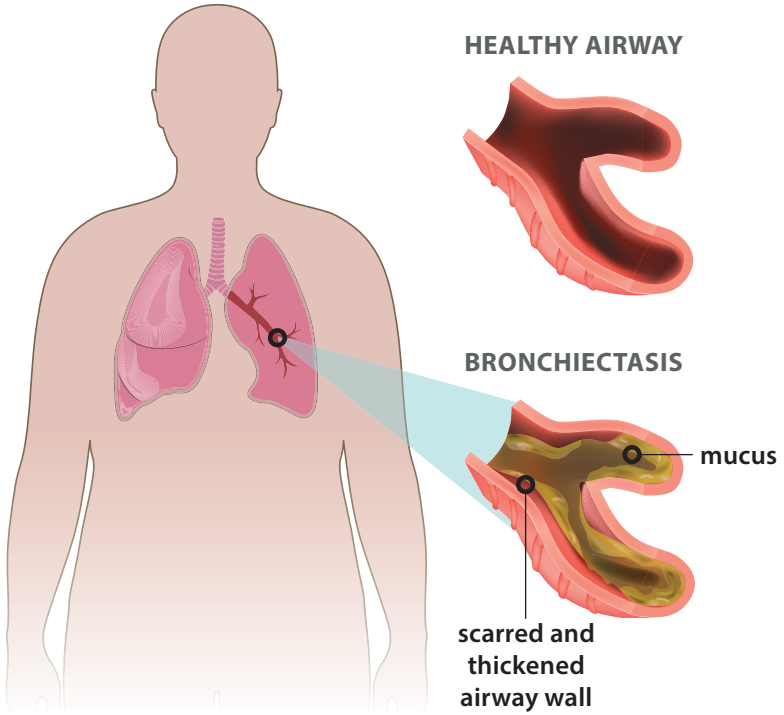
CHRONIC COUGH

In people with PCD, cilia do not beat properly, allowing mucus to build up in the lungs and making them prone to infections in the airways. This will often manifest as a chronic "wet" or "productive" cough, often starting quite early in life (even from birth) and daily mucus production, ranging from white, yellow to dark green phlegm.



SINUSITIS

Chronic, recurrent sinus infections (called sinusitis) are often seen as well, presenting as chronic nasal congstion, sinus pain, nasal polyps, headache and loss of smell. Chronic, recurrent ear infections also occur, mostly in children, but these can also continue into adulthood. Many PCD patients require repeat ear tube placement to drain ear fluid that can result in temporary or permanent hearing loss.



FERTILITY ISSUES

- **For women**
  Women may experience difficulty getting pregnant or have more risks for ectopic pregnancies (where the embryo implants outside of the uterus).

- **For men**
  Almost all men are infertile as their sperm do not swim properly (the sperm tail is a cilia-like structure).

However, both men and women with PCD can have normal children with fertility assistance, and genetic screening of partners, with help from genetic counselors, can predict the future risk of PCD in those children

// How is PCD diagnosed?

Making the diagnosis of PCD is often challenging. It can often be mistaken for asthma or chronic bronchitis or just bronchiectasis (i.e., irreversible airway dilatation or scarring) of unknown cause. Since PCD is an inherited condition, it is important to consider your family history of lung, sinus, or ear disease or reversed organs as possible indications for PCD.

There is no single test that can provide a reliable diagnosis for all cases. We rely on a series of different tests for the diagnosis of PCD:

CLINICAL HISTORY

Unlike other breathing disorders with similar symptoms, PCD symptoms almost always begin very early in life, often at birth, do not go away when the weather changes or respond well to standard asthma or allergy treatments. Wet cough and nasal congestion occur on a daily basis and never completely resolve, even with antibiotic treatment.

Review of the past medical history often reveals very frequent ear, sinus and lung infections. Some other targeted tests can also help with the diagnosis such as careful physical examination, sputum tests to examine for the typical bacteria seen in PCD, as well as a chest x-ray and very often a CT scan of the chest. Breathing tests will be helpful as well to assess the degree of airway disease.

CILIARY BIOPSY

A biopsy inside the nose can let us examine the internal structure of the cilia using transmission electron microscopy (TEM). This is one of the classic tests to diagnosis PCD. The biopsy is a minor procedure, done by scrapping ciliated cells from the surfaces inside the back of the nose. TEM is requires a high level of expertise not available at many hospitals, approximately 30% of people with PCD will have a normal TEM biopsy result.

NASAL NITRIC OXIDE TESTING

For reasons not yet fully understood, most people with PCD have extremely low levels of a gas called nasal nitric oxide (nNO) in their nose and sinus cavities. Over the past decade, research has shown that measuring nNO (a painless and quick test), can be useful for PCD screening and diagnosis.

GENETIC TESTING

There are over 50 different genes known to cause PCD, and most are included in commercially available genetic testing panels. However, since we do not yet know all the genes associated with PCD, a negative genetic test cannot rule out PCD. We estimate that PCD can be diagnosed by genetics in 70-80% of the cases.

// How is PCD followed and treated?

Although there is no specific treatment that helps the cilia work properly, there are treatments for the symptoms of PCD, including:

- **Antibiotic therapy** as needed to address the lung, ear or sinus infections.
- **Antibiotic prophylaxis** with Azithromycin to reduce bacterial load and inflammation locally. This was shown to significantly reduce the frequency of PCD respiratory exacerbations in both adults and children with PCD.
- **Airway clearance therapy** including breathing and coughing techniques, usually with the assistance of physical therapy or airway clearing devices (e.g., PEP, Aerokiba, Flutter valve, Acapella, etc). These techniques need to be done once to twice daily to help the lung stay clear of excess mucus and infection.
- **Vigorous exercise** can greatly augment or sometimes replace airway clearance therapies if done of a daily basis (i.e., cough during exercise is a good thing as it clears mucus very well and each deep breath during heavy exercise moves mucus out of the lungs).
- **Regular follow up with an otolaryngologist** (ear, nose and throat doctor) for ear and sinus issues is also critical to overall health in PCD. Some patients perform daily cleaning methods for the nose and sinuses (i.e., nasal/sinus rinses) or even need sinus surgery.

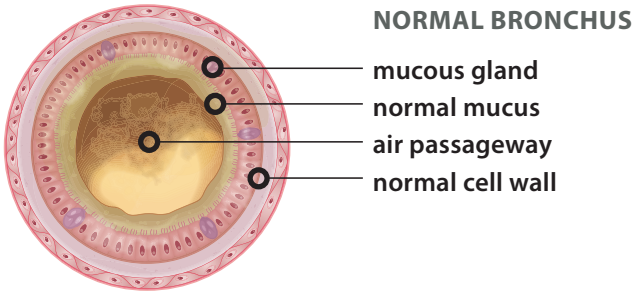
- **Airway clearance techniques** are often combined with inhaled therapies such as hypertonic saline solutions, inhaled antibiotics or both.
- New **PCD medicines** are being tested in research projects at the MUHC, and we hope to provide you access to promising, novel therapies soon

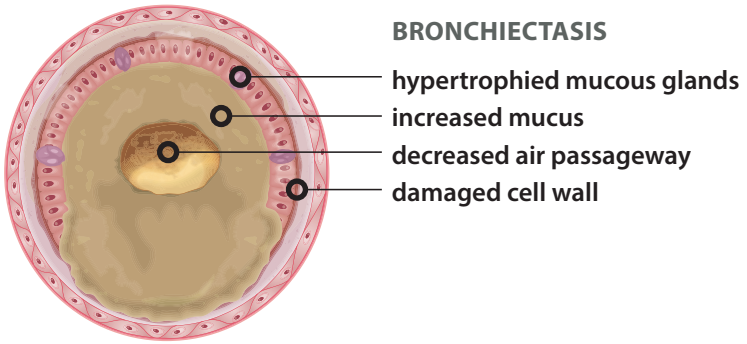
Prevention is key to good long-term outcomes in PCD, so it is important to see the doctor frequently (2 to 4 times annually), to have breathing tests and sputum tests frequently, to practice regular airway clearance, and to call your doctors anytime your respiratory symptoms are increased for more than a few days.

// What to expect?

Bronchiectasis

Over time, chronic inflammation and infection damage the airways permanently, causing irreversible widening and scarring called bronchiectasis (which may require a CTscan of the chest to be seen). By adulthood, nearly every person with PCD will have bronchiectasis.





- **Difficulty breathing**
  As bronchiectasis progresses, infections worsen and can sometimes lead to respiratory failure. Some people with advanced PCD may extra oxygen at night or during exercise or even require lung transplantation if their lungs become severly damaged.

There is currently no cure of PCD but there are several promising medical treatments that may slow its progress. While quality of life can be severely affected for people with PCD, there is a wide range of disease progression and long-term outcomes in patients; and there is no average "life expectancy".

// How do I manage PCD?

PCD requires daily management, like most chronic disease. The severity of PCD can vary greatly from person to person. The key is deciding whether you will manage the disease, or if the disease will manage you. Recurrent incretions tend to be unpredictable, and usually need antibiotic treatment.

In severe cases, you might need intravenous antibiotics for several weeks, either in hospital or in hospital at first and then home. Daily airway clearance therapy is also very important with the use of inhaled medications in some cases such as hypertonic saline solution or inhaled antibiotics.

// Can I participate in a study?

While PCD is not a new disease, we are still learning how to treat it. The MUHC has one of the largest PCD populations in the world, and this patient population has the power to change this disease by participating in research. At any time, there are several ongoing research projects for PCD patient involvement at the MUHC, including observational studies and clinical trials of novel medications and therapies.

We encourage each and every PCD patient to be involved in these efforts to transform PCD into a more manageable disease with improved outcomes.

Those interested in research participation should contact Dr. Adam Shapiro:

- by email — adam.shapiro@muhc.mcgill.ca
- by phone — 514-412-4444

// Other resources available

There are excellent sources of information and support groups to help you. We recommend that you visit these websites to read more about your condition and stay up to date with research opportunities, knowledge advancement and treatment options.

- MUHC PCD Clinic
  www.thechildren.com/departments-and-staff/departments/department-of-primary-ciliary-dyskinesia-pcd
- Regroupement Québécois des maladies orphelines
  www.rqmo.org
- PCD foundation
  www.pcdfoundation.org
- American Thoracic Society
  www. thoracic.org
- American Thoracic Society patient information series written by Dr. Shapiro
  www.atsjournals.org/doi/pdf/10.1164/rccm.1982P3
- National Organization for Rare Diseases (NORD)
  www.rarediseases.org

// Notes

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IMPORTANT: The information provided is for educational purposes only. It is not intended to replace the advice or instruction of a professional healthcare practitioner or to substitute for medical care.

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