Primary Ciliary Dyskinesia

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Primary ciliary dyskinesia (PCD) is an autosomal recessive disorder characterized by immotile, dysmotile, or absent cilia. The defect in ciliary motion leads to anomalous mucociliary clearance, resulting clinically in recurrent or persistent sinesorespiratory infections and infertility. Primary ciliary dyskinesia occurs in approximately 1 in every 20,000 to 60,000 individuals in the United States, although this is likely an underestimate of the actual incidence.

There is considerable variability in the clinical presentation of PCD, leading frequently to delays in diagnosis. The symptoms of PCD correspond to the organs where ciliary motility is a crucial component of normal function. Upper and lower respiratory tract involvement is common. Neonatal respiratory distress, often attributed to transient tachypnea of the newborn or neonatal pneumonia, is frequently seen retrospectively in patients later diagnosed as having PCD. Recurrent pneumonia and bronchiectasis can be seen in young children. Chronic persistent rhinosinusitis is almost universally present in patients with PCD. Nasal polyps are frequently seen. Because of abnormal ciliary function in the eustachian tubes, children with PCD frequently have recurrent acute otitis media and chronic serous otitis media with the risk of conductive hearing loss. After childhood, men with PCD are infertile secondary to immotile spermatozoa. Adult women with PCD have an approximately 50% risk of infertility due to impaired ciliary function in the fallopian tubes impairing the travel of the ovum. Similarly, women with PCD are at increased risk for ectopic pregnancy. Radiographically, patients with PCD can have peribronchial thickening, atelectasis, and air trapping that can contribute to bronchiectasis. In contrast to patients with cystic fibrosis, who often have abnormalities more evident in the upper lobes, patients with PCD typically have abnormal radiographic findings more prominent in the middle and lower lobes.

Approximately 50% of patients with PCD have situs inversus totalis. The triad of situs inversus totalis, chronic sinusitis, and bronchiectasis is referred to as Kartagener syndrome, a subgroup of PCD. Normal ciliary function is necessary to control the typical laterality of the heart during embryologic development; in individuals with PCD and resultant impaired ciliary function, that laterality is not obligatory, leading to the 50% odds of situs inversus.

The diagnosis of PCD is frequently delayed because the cardinal symptoms—recurrent sinusitis, chronic rhinitis, and recurrent otitis media—are also frequently seen in otherwise healthy children. Spirometric findings can be normal in early childhood, but some degree of airflow obstruction is typically seen as a child ages. To ultimately diagnose PCD, one needs the identification of ciliary dysmotility which requires specialized techniques and expertise often best accomplished in a tertiary diagnostic center. Ciliated cells can be obtained from the nose or trachea by brushings or mucosal biopsy with subsequent examination of ciliary ultrastructure by electron microscopy. Genetic testing is evolving but can be
problematic due to genetic heterogeneity and the large number of potential genes involved.

Treatment modalities are focused on symptom management because there are no current therapies available to correct the underlying ciliary dysfunction at the cellular level. Respiratory management includes airway clearance involving chest physiotherapy and exercise and aggressive identification and treatment of upper and lower airway infections. Environmental protections should include avoidance of active and passive tobacco smoke exposure. Patients with PCD should receive all recommended childhood vaccinations as well as the pneumococcal polysaccharide vaccine and annual influenza vaccine.

**COMMENT:** This *In Brief* reviews critical aspects of recognition for PCD. Because cilia are present in the middle ear, eustachian tubes, nares, paranasal sinuses, nasopharynx, trachea, bronchi, and reproductive tracts of men and women, all of these anatomical areas may be affected with ciliary dysfunction. It is imperative to rule out cystic fibrosis when evaluating patients with these symptoms. In a study comparing patients with PCD and those with neonatal respiratory distress (most commonly transient tachypnea of the newborn), those with PCD were more likely to present with respiratory distress at a later onset (median of 12 hours compared with 1 hour), to have oxygen requirements for more than 2 days, and to demonstrate lobar collapse on chest radiography. Primary ciliary dyskinesia is a complex diagnosis because there is no one diagnostic test with perfect sensitivity or specificity. Hence, referral to 1 of the 7 current clinical research sites within the Genetic Disorders of Mucociliary Clearance Consortium (http://rarediseasesnetwork.epi.usf.edu/gdmcc/index.htm) is strongly recommended for patients meeting the risk factors for further evaluation and diagnosis.

– Janet R. Serwint, MD
Associate Editor, *In Brief*

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