

THE BEAT



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Dates to Remember

May 19-25 ATS Conference

May 20-21 Alternate PCD Walk-a-Thon Date

August 11-12 PCD Family Education Day

February 4-9, 2007 Gordon Conference on Cilia, Mucus, and Mucociliary Interaction

Did You Know...

- Certain types of cilia are implicated in other disorders such as polycystic kidney disease and Bardet-Biedl syndrome? For more information on cilia-related disorders, see Journal Watch on page 4.
- A genetic test for some PCD mutations (mostly affecting outer dynein arms) will soon be available? See page 3 for details.

PCD at ATS

The American Thoracic Society (ATS) annual conference will be held May 19-25 in San Diego, California. This meeting is the largest gathering of pulmonary health professionals and researchers in the country and the projected attendance this year is 17-20,000 international participants. The meeting covers all aspects of respiratory disease and management, but this year several events will focus on primary ciliary dyskinesia, including updated information on genetics, research and clinical management. Margaret Leigh, MD will be hosting the third annual workshop of PCD investigators whose goal is to create PCD treatment guidelines for publication. In addition, there will be a scientific symposium dedicated to research updates in PCD. This symposium will feature speakers from the international PCD research community and will also include a patient speaker, Meghan Manion, to address the impact of PCD from the patient perspective. A PCD case study will also be presented in a "Grand Rounds" session and clinicians will be asked to guess the disorder based on history. This session is followed by an in-depth discussion on recognizing the clinical signs of PCD.



PCD Group Enjoying the San Diego Sun at ATS 2005

The ATS meeting is also an opportunity for researchers to present new, unpublished findings. These presentations frequently take the form of "poster" sessions. The posters are visual aids allowing researchers to fit a great deal of information into a relatively small area (about the size of a large commercial poster). There will be a number of poster presentations dedicated to PCD this year.

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PCD Study Ready to Register Patients

The Genetic Disorders of Mucociliary Clearance Consortium (GDMCC) study is now registering PCD patients. The GDMCC is one of 10 rare disease consortia established by the National Institutes of Health and the Office of Rare Diseases to encourage research in diseases that affect a small number of individuals. PCD, atypical cystic fibrosis and pseudohypoaldosteronism (PHA) are the diseases represented in the GDMCC, with PCD being the primary focus for initial patient enrollment.

There will be a number of opportunities for patient participation in GDMCC projects

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PCD Study

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and all patients are encouraged to register with the GDMCC. Please note that registering with the consortium is not the same thing as enrolling in a study. The registration process is designed to compile a list of patients interested in and willing to participate, who will then be matched with appropriate study opportunities as they arise.

A downloadable version of the registration form is available at the Rare Diseases Clinical Research Network website: <http://rarediseasesnetwork.epi.usf.edu/gdmcc/index.htm> by clicking on the link to the paper form or you can register online at this site by clicking on the "Join the Contact Registry Button." Forms can also be downloaded from the PCD Foundation website: www.pcdfoundation.org or you can contact the Foundation for a hard copy. Please fill out a separate copy of the form for each affected individual.

Once you have registered, Susan Minnix, RN, Research Nurse Coordinator for the GDMCC project has asked that you notify her or Beth Godwin, Research Administrator of your interest in participating either via e-mail or by fax.

Susan: Email: sminnix@med.unc.edu
Fax: 919-843-5309

Beth: Email: godwine@med.unc.edu
Fax: 919-966-7524

PCD at ATS

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In addition to the formal PCD events at ATS this year, we will also be participating in forums focused on bronchiectasis, airway clearance options, lung transplantation and other respiratory topics of interest to the PCD community.

To take advantage of the attention on PCD at ATS this year, the PCD Foundation will have an exhibit booth staffed by patients and families with information on the Rare Diseases Clinical Research Network, the Foundation, and a video featuring clips of normal and PCD cilia and biopsy information.

PCD Get-together at ATS

We will be having an informal luncheon for patients, families, friends, health care providers or anyone interested in PCD on Saturday, May 21 at noon. If you would like to attend, please contact Michele at the PCD Foundation (info@pcdfoundation.org or 612-396-1179) for more information.

THANK YOU AIG!
The PCD Foundation's appearance at ATS 2006 is being sponsored, in large part, by a generous donation from American International Group (AIG). We are very grateful for their support of this event.

2006 PCD Family Education Day

Make plans to join us for the Fourth Annual PCD Family Education Day, August 11-12, 2006 at the Millennium Hotel in Buffalo, New York. Family Day this year, as in the past, will feature speakers on pulmonary and ENT issues in PCD, ciliary structure and function, updates on research and genetic testing, and psychosocial issues in PCD. An added feature this year will be guest speaker Sharon Dell, MD from the Hospital for Sick Children in Ontario, Canada who will share her experiences with developing a PCD clinic in Toronto.

We are looking forward to a big group this year and we will have the opportunity to meet with our PCD friends from Canada. There is a discount for early registration. For more information, check the PCD Foundation website at www.pcdfoundation.org or contact Lynn Ehrne at linnie1@frontiernet.net



Group Photo Family Day 2005, St. Louis

Family Day is a great opportunity to learn about PCD, have your questions answered by professionals, find support and guidance, and to enjoy meeting with new friends. We hope to see you there!

Update on PCD Genetics

An area of intense focus for PCD researchers is identifying the genetic mutations responsible for primary ciliary dyskinesia and other cilia-related disorders. Genes are units of information carried on the genetic material (DNA) inherited from our parents. Genes encode for the proteins that build every cell, tissue, and organ in the body and the interaction of genes and their protein products help regulate complex body functions. There are more than 600 proteins involved in the production of a functioning cilium (including basal body), however, not all of these proteins are implicated in ciliary dyskinesia. Part of the challenge for genetic researchers is to determine which genes are likely to be disease causing. These "candidate" genes are then examined closely for mutations. Once a gene is identified as disease-causing, it is necessary to find the specific area of code on the gene that contains the mutation. A mutation is an alteration in the code that interferes with the production or expression of the correct protein. PCD is a condition that is passed recessively (for the most part) meaning that affected individuals inherited protein-altering mutation from each parent.

Why Genetic Research is Important:

- **Early diagnosis**
- **Potential for new therapies**
- **Access to "personalized" medical care**
- **Determination of carrier status**

Genes contain large amounts of information—sometimes enormously large amounts. This information is divided into smaller units called exons. Some genes have a relatively small number of exons, some have a very large number of exons. Two genes have been implicated in PCD and there are a number of candidate genes currently under investigation. Mutations in both of the known genes, DNAI1 and DNAH5, interfere with the production of proteins involved in making outer dynein arms (ODAs). While there are only two known PCD genes, more than 40 distinct disease-causing mutations have been identified on these genes so far—practically a separate mutation for every family!

Currently, blood screening for genetic diseases relies on identifying known defects in the exons. Cystic fibrosis (CF) provides a good example of how genetic testing works. CF is a single gene disorder, but more than 1200 distinct mutations have been identified on this single gene. In the early days of genetic testing for CF, the standard test looked for mutations in 30 exons and the best test looked for mutations in 90 exons. Granted, these were the most common CF mutations, but the tests left plenty of room for false negative and/or inconclusive results. Newer CF genetic tests look for over 1,000 separate CF mutations, a dramatic improvement, but still not 100%.

A genetic assay for some of the known mutations in PCD is currently being used in the research setting and efforts are underway to make this technology available to medical professionals in non-research settings. This is an exciting development for PCD diagnosis and treatment. However, it is an initial step and there are some important things to remember: First, the initial blood test for PCD will be looking at only 9 exons—the 9 most common areas of mutation. It is expected that this will pick up the majority of DNAH5 and DNAI1 mutations, but some will be missed. Vigorous international effort is being expended to identify the genes involved in inner dynein arm defects and in less common ciliary abnormalities such as radial spoke defects, central apparatus defects and ciliary aplasia. Because there are no known mutations related to these defects, genetic testing will not be an effective diagnostic tool in these cases. The goal is to continually add mutations to the screening panel as they are identified. Second, this is an expensive procedure. Screening for each exon costs about \$100 (break even cost—no profit) and there is an additional fee for DNA extraction and prep, as well. This means the initial screening test for PCD will be approximately \$1200 or more. Because it is anticipated that the test will be approved for use by certified professional labs (CLIA designation) insurance should cover the cost of the test. This is also an opportunity for us to advocate for PCD by supporting PCD genetic testing with our personal insurance companies. In addition, the PCD Foundation is in the process of petitioning the World Health Organization for a diagnostic code which, if granted, should facilitate insurance coverage.

Unraveling the genetic picture is crucial for more than just diagnostics. We are entering the age of "genomic" medicine and soon it may be possible to personalize treatment plans based on individual genetic profiles. For example, in our group we have observed that some members seem to do better overall than others and that patients respond very differently to standard therapies. Genetic medicine may help explain these differences and provide guidelines that will determine the best care for each individual. While not mainstream yet, this style of medicine is already being used to determine individual medication dosages for some drugs. The potential applications are very exciting. Related to this is the possibility that genetic information may make it possible to predict disease course and outcome based on genetic profile or genotype. If you think of your genotype as the set of instructions that were used to produce you, then your phenotype is the finished product—the physical expression of the traits (e.g. blue eyes, brown hair, crossed toes, etc.) coded in your genotype. For PCD researchers studying genotype/phenotype correlation—how specific genetic mutations are expressed in the disorder known as PCD—this information may lead to a better understanding of the course and severity of disease. For instance, if it becomes clear that certain mutations are associated with mild disease or with severe disease, therapy could be tailored to fit the needs of the individual patient with those mutations. Also, PCD is primarily passed as a recessive trait, so knowing the specific mutation in your family can be useful for identifying carriers, if desired.

Genetics is a complex and fascinating field. For more information and a great glossary of terms check out The Genome News Network at: <http://www.genomeneetwork.org/>.

A Publication of the PCD Foundation

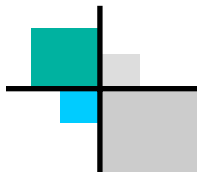
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We're on the Web!!!

www.pcdfoundation.org

*Education & Advocacy for
People with Inherited Ciliary
Disorders*



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Journal Watch NEW ARTICLES OF INTEREST TO THE PCD COMMUNITY

The National Library of Medicine (NLM) maintains a database of peer-reviewed articles from international medical journals. The peer-review process means that the article is subject to vigorous critical review by a panel of experts prior to being accepted for publication. This information can be accessed by the public at:

<http://www.ncbi.nlm.nih.gov/PubMed> or by typing "entrez pubmed" into your internet provider search function.

When you enter a query (e.g. primary ciliary dyskinesia) into PubMed, a list of articles will appear, most recent at the top. Click on each article for a link to its **abstract**, or brief overview. Often, the abstract provides enough information and there is no need to get the full article. If the full article is desired, there are several ways to obtain it; 1.) universities with medical schools frequently maintain a large inventory of medical journals. Copies of articles from these journals are usually available to the public for a small fee, 2.) articles can be ordered from the publisher for a (typically large) fee, and 3.) the PCD Foundation maintains a bibliography of many articles and may be able to provide single copies for educational purposes.

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