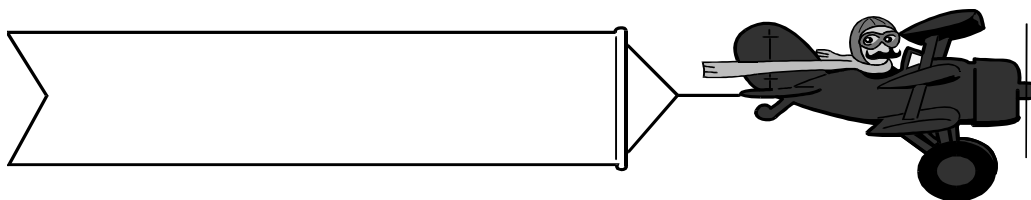

REGISTRY NEWS

Volume 8 Newsletter for the Pediatric Cardiomyopathy Registry

Winter 1999



We thank all centers for their excellent job of enrolling patients and completing the follow-up forms. We are drawing some exciting conclusions, as we analyze our first set of data. As we would like to include your site in our database, and the deadline for data submission is **April 1999**, we encourage you to submit your data as soon as possible. If you need some assistance meeting the April deadline, please contact *Eran Muto* or *Kristen Lewis* at the PCMR Administrative Coordinating Center at (716) 273-2159 or (716) 275-2238, respectively.

Attention Prospective Sites in New England and the Central Southwest

For centers in Massachusetts, Connecticut, Rhode Island, Vermont, New Hampshire, Maine, Texas, Oklahoma, and Arkansas, we will call you to obtain the following data: **all newly diagnosed patients with cardiomyopathy at your institution since January 1, 1996.**

- We need to complete a prospective enrollment form for each of your new patients.
- When we contact you, we will review whether your center has enrolled patients newly diagnosed since 1996 but have not yet had supplemental enrollment form (*Form 02*) data submitted. If this is the case, we ask that you submit the completed supplemental enrollment form within the next two weeks. If you would like assistance, an Outreach Visit can be arranged.

Attention Retrospective Sites

For centers throughout North America who have enrolled patients newly diagnosed with cardiomyopathy between January 1, 1990 and December 31, 1995, we will contact you this month if you have any outstanding forms. You will be receiving updated patient status reports from the Data Coordinating Center in the near future. These reports list outstanding forms and edit reports to give you a better idea of which data are still expected and for which patients.

- Some patients may need their supplemental enrollment form (*Form 02*) completed or have outstanding edit reports. The above mentioned list will indicate by ID number what patients are in these two categories.
- When we call, we will ask whether your site is interested in scheduling an Outreach Visit, whether you can update us by phone, or whether you are willing to complete the data collection yourselves.
- If you prefer that we visit your site to complete the outstanding forms, it helps us tremendously if you pull the appropriate medical records in advance.

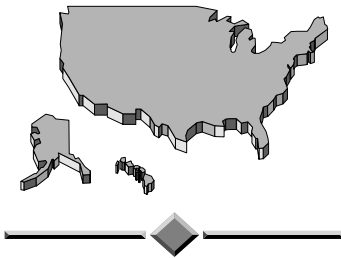
Once again, thank you for your assistance. Your contributions to the PCMR are coming to fruition. We hope to share some preliminary findings with you in the next newsletter.



ENROLLMENT REPORT

PCMR Enrollment as of January 27, 1999 1,965 Eligible Patients

As of January 27, 1999 we have **1791** eligible patients enrolled in the Registry!



Of the 182 sites that have agreed to participate, the following 85 sites have submitted Enrollment Forms:

- Duke University, Durham, NC, *Dr. Resai Bengur*
- Strong Memorial Hospital, Rochester, NY, *Susan Truesdell, P.A.*
- University of Maryland Medical System, Baltimore, MD, *Dr. Janet Scheel*;
- Oregon Health Sciences University, Portland, OR, *Dr. Mark Reller*
- Babies and Children's Hospital, New York, NY, *Dr. Daphne Hsu*
- The Children's Heart Center of West Texas, Lubbock, TX, *Dr. Charlie Sang*
- TC Thompson Children's Hospital, Chattanooga, TN, *Dr. John Morgan*
- Children's Hospital, Buffalo, NY, *Dr. Robert L. Gingell*
- St. Louis Children's Hospital, *Dr. Arnold Strauss and Dr. Vernat Exil*
- University of Iowa Hospitals and Clinics, Iowa City, IA, *Dr. Mary Jeannette Hagan Morriss*
- The Hospital for Sick Children, Toronto, Ontario, Canada, *Dr. Lee Benson*
- Children's Hospital of Los Angeles, *Dr. Alan B. Lewis*
- Primary Children's Medical Center, Salt Lake City, UT, *Dr. Bob Shaddy*
- Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, *Dr. Martin Hosking*
- University of Texas Medical Branch, Galveston, TX, *Dr. William Pearl*
- Children's Associated Medical Group, San Diego, CA, *Dr. Rob Spicer*
- Vanderbilt University, Nashville, TN, *Dr. Debra Dodd*
- Mt. Sinai Medical Center, New York, NY, *Dr. Bruce Gelb*
- Michigan State University, East Lansing, MI, *Dr. Monica Goble*
- NYU Medical Center, New York, *Dr. Michael Artman*
- Children's Hospital of Wisconsin, Milwaukee, *Dr. Stuart Berger*
- Children's Hospital, Omaha, NE, *Dr. Ameeta Martin*
- Dartmouth-Hitchcock Medical Center, NH, *Dr. Nancy Drucker*
- Yale University, *Dr. Peter Bowers*
- University of Alberta Hospital, Edmonton, Alberta, Canada, *Dr. John Dyck*
- Children's Hospital of Michigan, Detroit, MI, *Dr. Robert Ross*
- Tulane University Hospital and Clinic, New Orleans, LA, *Dr. Arthur Pickoff*
- UC Davis Medical Center, Sacramento, CA, *Dr. Mark Parrish*
- Capital District Pediatric Cardiology Assoc., P.C., Albany, NY, *Dr. Eric Spooner*
- Texas Children's Hospital, Houston, TX, *Dr. Jeffrey Towbin*
- Children's Hospital, Boston, MA, *Dr. Steven Colan*
- Metro Health Medical Center, Cleveland, OH, *Dr. David Connuck*
- Elliot Hospital, Manchester, NH, *Dr. Sol Rockenmacher*
- Rhode Island Hospital, Providence, RI, *Dr. John Werner*
- Children's Hospital of Pittsburgh, PA, *Dr. Steve Webber*
- Connecticut Children's Medical Center, Hartford, CT, *Dr. Harris Leopold*
- Hasbro Children's Hospital, Providence, RI, *Dr. Robert Corwin*
- Children's Hospital Medical Center, Cincinnati, OH, *Dr. Tom Kimball, Dr. William Lewis, and Dr. David Schwartz*
- Loma Linda University Medical Center, Loma Linda, CA, *Dr. Ranae Larsen*
- UCSD Medical Center, San Diego, CA, *Dr. Abraham Rothman*
- Children's Memorial Hospital, Chicago, IL, *Dr. Elfriede Pahl and Dr. Sam Gidding*
- Cleveland Clinic Foundation, OH, *Dr. Maryanne R. Kichuk*
- Johns Hopkins School of Medicine, Baltimore, MD, *Dr. Vicente Lemes*
- University of Texas Health Science Center, Houston, TX, *Dr. Steven Wolfe*
- University Hospital, Oklahoma City, OK, *Dr. Kent Ward*

(Continued on next page)

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- Children's Medical Center of Dallas, TX, *Dr. Matthew S. Lemler*
- UMASS Medical Center, Worcester, MA, *Dr. Phyllis Pollack*
- Children's Hospital Heart Center, Albuquerque, NM, *Dr. J. Deane Waldman*
- University of Kentucky College of Medicine, Lexington, KY, *Dr. Bradley Keller*
- Marshall University School of Medicine, Huntington, West Virginia, *Dr. Mahmood Heydarian*
- Wichita Clinic of Kansas, *Dr. Steve W. Allen*
- New York Hospital, Cornell Medical Center, New York, NY, *Dr. Myles Schiller*
- University of Miami School of Medicine, Miami, FL, *Dr. Delores Tamer*
- University of Florida, Gainesville, FL, *Dr. F. Jay Fricker*
- Montefiore Medical Center, Bronx, NY, *Dr. Carl Steeg*
- Pediatric Cardiology, San Antonio, TX, *Dr. Kenneth Bloom*
- Loyola University Medical Center, Maywood, IL, *Dr. Elizabeth Fisher*
- Presbyterian Professional Building, Dallas, TX, *Dr. Ed Neufeld*
- Cook Children's Heart Center, Fort Worth, TX, *Dr. J. Hudson Allender and Dr. Steve Lai*
- Healthcare Professional Associates, Amarillo, TX, *Dr. Jorge Garcia*
- The Children's Heart Clinic, Minneapolis, MN, *Dr. Robert Gajarski*
- East Carolina University School of Medicine, Greenville, NC, *Dr. Michael McConnell*
- Children's Hospital of Orange County, CA, *Dr. Melville Singer*
- Texas Tech University, El Paso, TX, *Dr. Jeffrey Schuster*
- Children's Cardiology Associates, Austin, TX, *Dr. Stuart Rowe*
- Arkansas Children's Hospital, Little Rock, *Dr. Elizabeth Frazier and Dr. Paul Seib*
- PEDIAPEX Heart Center for Children, Dallas, TX, *Dr. Lee Ann Pearse*
- Wilford Hall Medical Center, Lackland Air Force Base, TX, *Dr. John Brownlee*
- Alberta Children's Hospital, Calgary, Canada, *Dr. David Patton*
- Univ. of Alabama, Birmingham, *Dr. Bennett Pearce*
- Pediatric Cardiology Associates, Portland, ME, *Dr. Maribeth Hourihan*
- Children's Heart Network, San Antonio, TX, *Dr. James Rogers*
- Pediatric Cardiology, Bayside Medical Building, Providence, RI, *Dr. Patricia Rompf*
- Massachusetts General Hospital, Boston, MA, *Dr. Baruch Ticho*
- Royal University Hospital, Saskatoon, SK, Canada, *Dr. Michael Tyrrell*
- BC Children's Hospital, Vancouver, BC, Canada, *Dr. Derek Human*
- Boston Floating Hospital, MA, *Dr. Jonathan Rhodes*
- Driscoll Children's Hospital, Corpus Christi, TX, *Dr. John Pastorek*
- Children's Hospital of Montreal, Quebec, Canada, *Dr. Charles Rohlicek*
- University of Illinois Medical Center, Chicago, IL, *Dr. S.P. Kumar*
- Eastern Maine Medical Center, Bangor, ME, *Dr. Angela Gilladoga*
- Medical College of Virginia, Richmond, *Dr. William Moskowitz*
- Children's Heart Center, Las Vegas, NV, *Dr. William Evans*
- SUNY Downstate Medical Center, Brooklyn, NY, *Dr. Dov Nudel*
- UCLA Children's Hospital, Los Angeles, CA, *Dr. Samuel Kaplan and Dr. Juan Alejos*

Please submit your Enrollment Post Cards as soon as possible. Every contribution strengthens the database of information for future use in clinical and scientific environments.



DATA MANAGER CORNER

The following are a few important things to remember before sending data to the DCC:

- 1) Make sure **ALL** questions are answered on the data collection forms, even if the answer is "No." If you **cannot** answer a question, write a *brief* explanation in the margin as to why you left it blank. Please write legibly! I think edit reports are as much of a nuisance as you do!
- 2) If a transplant was performed during the year of a requested Annual Follow-Up Form, only *pre*-transplant information is requested. No further Annual Follow-Up Forms should be completed after the year of transplant.
- 3) A W-9 form is necessary to receive reimbursement for forms completed and returned to the Data Coordinating Center. Please complete and send them to the Administrative Coordinating Center in Rochester, NY, attention Kristen Lewis. It should take two weeks for checks to be processed - reports are run at the end of every month.
- 4) Once the initial Enrollment Post Card has been sent to the DCC, a pre-labeled Supplemental Enrollment Form (02) will be forwarded to your site. This form serves as a compliment to the initial enrollment form, and should be submitted at the earliest opportunity to complete the database on the new patient. Pre-labeled Annual Follow-Up Forms (03) will be forwarded to sites for each enrolled

patient at the yearly anniversary of the date of diagnosis. This form should be submitted within a one month window of the patient's annual follow-up date.

5) If a patient does **NOT** meet the inclusion criteria (question 8 on the enrollment postcard), the patient is ineligible for the registry. Please do not send postcards for these patients to the DCC.

6) It is extremely important that the ID assignment log is kept in a secured and well-organized place at each site. (Never send this log to the DCC as it contains the names of patients. Remember, patient confidentiality is crucial!) This log is the only link in the registry between ID #'s and patients. **DO NOT LOSE IT!!!**

My phone number is (617) 923-7747 ext. 366. Please leave a message on my voicemail if I do not answer, and I will get back to you as soon as possible. You can fax or e-mail requests for additional forms and labels to Kristen Noonan at (617) 926-0144 or KNoonan@neri.org.

Thank you for your continuing effort to keep the Pediatric Cardiomyopathy Registry as complete and accurate as possible.

FREQUENT QUESTIONS ... ANSWERED!



Q: *There is no code for this particular diagnosis, what should I do?*

A: If there is no diagnosis code available for the diagnosis of a patient on the Enrollment Form, please write a brief diagnosis name in the blank area (i.e., viral myocarditis, IDCM with EFE, etc.).

Q: *What is the reporting period for the Supplemental Form (02)?*

A: The reporting period is listed on the label attached to the top right corner of the form. Results recorded on the Supplemental Form should be from tests and procedures done at the time of diagnosis.

Q: *What if there are several tests and procedures done over the period of a year - which do we record on the Annual Follow-Up Form (03)?*

A: The reporting period is listed on the label attached to the top right corner of the form. Results recorded on the Annual Follow-Up Form should be from the most recent tests and procedures during the year requested. (For example, if 09/96 - 09/97 is requested, then tests taken in

August 1997 as opposed to those taken in December of 1996 would be documented.) However, if the patient has become acutely ill during the reporting period, please record these test results instead.

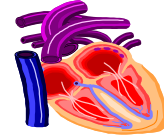
Q: *I don't have the time to complete the follow-up forms. Who can help me?*

A: Consider having a nursing student, medical or patient technician, or someone with a medical background. To attract such an individual consider a flexible working arrangement (i.e., flex hours, an autonomous environment, and an adequate and appropriate compensation).

Q: *Where on the follow-up forms do we indicate if a patient's cardiomyopathy has resolved?*

A: If a patient's cardiomyopathy has resolved and is no longer present, please answer "**no**" to the question, "*Is cardiomyopathy present at this time?*" (Function Type of Cardiomyopathy section) on the appropriate annual follow-up form.

RELEVANT ARTICLE SUMMARY



Impact of Laboratory Molecular Diagnosis on Contemporary Diagnostic Criteria for Genetically Transmitted Cardiovascular Diseases: Hypertrophic Cardiomyopathy, Long-QT Syndrome, Marfan Syndrome

A Statement for Healthcare Professionals from the Councils on Clinical Cardiology, Cardiovascular Disease in the Young, and Basic Science, American Heart Association

B.J. Maron, MD, Chair; J.H. Moller, MD, Cochair; C.E. Seidman, MD; G.M. Vincent, MD; H.C. Dietz, MD; A.J. Moss, MD; J.A. Towbin, MD; H.M. Sondheimer, MD; R.E. Pyeritz, MD, PhD; G. McGee, PhD; A.E. Epstein, MD
Circulation 1998; 98: 1460-1471

Hypertrophic Cardiomyopathy

The diagnosis of HCM in most affected adult patients is most easily and reliably established by clinical examination, including a careful 2-dimensional echocardiographic imaging. In instances where clinical diagnosis is certain, establishing the genetic defect responsible for the disease by DNA analysis represents only a diagnostic confirmation. However, molecular studies have the potential to enhance diagnostic reliability. With the use of genotyping, it is possible to resolve ambiguous diagnoses of HCM, such as when phenotypic expression is more subtle. HCM can be caused by a mutation in any 1 of 5 genes that encode proteins of the cardiac sarcomere: beta-myosin heavy chain (on chromosome 14), cardiac troponin T (chromosome 1), troponin I (chromosome 19), alphasarcomyosin (chromosome 15), and cardiac myosin-binding protein C (chromosome 11). Mutation in 2 genes

encoding essential and regulatory myosin light chains have been reported in what may be an extremely rare form of HCM. In addition, the availability of DNA-based diagnosis has led to the identification of increasing numbers of children and adults with a preclinical diagnosis, usually in the context of genetic testing in selected pedigrees. These individuals have a disease-causing genetic mutation but no clinical or phenotypic manifestations of HCM, such as left ventricular wall thickening on echo or cardiac symptoms. On the basis of available data, it appears likely that most such genotype-positive, phenotype-negative children will develop left ventricular hypertrophy while achieving full body growth and maturation. In comparison, few genetically affected adults have been reported to show little or no left ventricular hypertrophy. The frequency and timing with which these adults may develop clinical signs of HCM is unknown.

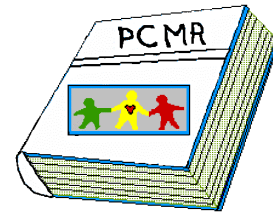
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Pediatric Cardiomyopathy Registry

Informational Session at the American College of Cardiology Convention

Monday, March 8, 1999
7:00 am to 8:00 am

New Orleans Marriott
555 Canal Street
New Orleans, Louisiana



While working on the renewal, we have conducted several interesting analyses.
We will be discussing this new data at the meeting. Please save the date!

(Continued from previous page.)

Long-QT Syndrome

The diagnosis of LQTS has traditionally been made based on the measurement of the QT-interval duration on 12-lead ECG, whose accurate interpretation is subject to a number of practical obstacles. Molecular diagnosis has the potential to overcome some of these inherent difficulties and enhance diagnostic reliability in LQTS. Available genotype-phenotype correlations in LQTS indicate that a normal QTc does not exclude the disease. When false-negative, false-positive, and borderline values are combined, uncertainty may exist in as many as 50% of family members clinically diagnosed using QTc measurement. Molecular diagnosis would potentially be most informative for this group of relatives in LQTS families.

At present, 4 mutant genes encoding proteins of the cardiac ion channels have been identified as responsible for LQTS. A fifth locus on chromosome 4 has also been reported, but the gene has not yet been identified. In addition, substantial intragenic heterogeneity has been established for

LQTS, with >30 total mutations (mostly missense) now described in ~40 families. Given this marked genetic heterogeneity of LQTS, the possibility of comprehensive screening for LQTS genetic defects seems particularly difficult.

Marfan Syndrome

MFS remains a clinically diagnosed disease, despite the variability in expression and diagnostic complexities often associated with accurate assessments. No genetic test used in isolation is available for definite assignment of either affected or unaffected status for MFS.

A defect in the FBN1 gene has been found to be responsible for MFS. Since such substantial allelic heterogeneity is evident within the fibrillin gene, the development of a routine screening process to establish a diagnosis of MFS would be difficult. Therefore, molecular data should not be used as the sole determinant in the diagnosis of MFS, but in conjunction with a clinical assessment of the MFS phenotype.

The Year of the Transgenic Mouse

I recently sat down with the 1998 American Heart Association abstracts, curious to see what were the current interests in research relevant to the cardiomyopathies. Of the 4551 abstracts in this thick volume on every aspect of cardiovascular disease, 104 were indexed under “cardiomyopathy”. Being retired, with the luxury of time, I paged carefully through and found another 65 I considered relevant. The surprisingly large total shows a growing interest in the subject. I scanned through them, not to do any scientific critique, but merely to identify the objectives. The investigations were about equally divided between human and animal.

A few of the **human** studies I considered noteworthy follow (with abstract numbers):

- New or more detailed gene characterizations in dilated cardiomyopathy (1270, 1277, 1552, 3127, 3129, 3130, 3288), and in hypertrophic cardiomyopathy (1271, 1273, 1276, 2661, 2662, 3133).
- Echocardiographic findings of possible value: loss of 3-layer appearance of the myocardium and displacement of main septal perforator in HCM (4451), ultrasonic tissue characterization in DCM (831, 2264).
- Regarding the role of immune mechanisms in DCM, autoantibodies were found early (378). T-lymphocyte activation correlated with progression (1095), and immunoabsorption treatment was evaluated (528, 529).
- Cardiac complications of congenital HIV (3249).
- Treatment efforts included: for DCM, growth hormone (1287, 3048); for HCM with obstruction, septal artery alcohol injection (436, 1576, 2272, 2334, 2656, 2659, 4402) and dual chamber pacing (2658, 3749); mechanical support for end-stage failure (3240, 3935).

The **animal** studies were exciting. While in earlier years the only animals that could be studied were spontaneously cardiomyopathic hamsters and cats, today we have the cardiomyopathic animals, mostly mice, produced by genetic engineering to have overexpression or deletion of relevant genes (43 abstracts!). Many of the overexpressed ones were of human origin.

The “Holy Grail” would seem to be the ability to diagnose and specifically treat the diverse etiologies of genetic cardiomyopathies even as new mutations appear. Today’s investigators seem to be well on the way. And as we approach this goal, the pooling and sharing offered by this Registry should become even more important.

Paul R. Lurie, MD



Important Notes

There is a new *Administrative Coordinator*. Kristina McCoy has left. Please send all future correspondence to:

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University of Rochester
601 Elmwood Ave., Box 631
Rochester, NY 14642

Tel: (716) 275-2238

Fax: (716) 275-7436

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Registry News

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Registry News

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