

CYSTIC FIBROSIS CENTER

NEWS

WINTER/SPRING 2010

Packard Children's Hospital Setting a High Bar: Newborn Screening Programs



Bailey Family: Barclay, Katherine, David, Reid and Gregory. (l to r)

The year 2009 was a milestone for the future of cystic fibrosis (CF) in the U.S. It marked the first year when every state in the U.S. provided or planned to provide newborn screening (NBS) for the disease. California began its NBS program in July 2007. We are only beginning to understand the positive effect that early diagnosis followed by appropriate treatment will have on the course of CF. Optimism appears justified.

During the first two years of screening in California, 429 newborns had a positive test, with 156 confirmed cases. California's comprehensive NBS program screens for 76 genetic diseases, using a blood spot from a "heel stick" soon after birth. The California CF test uses both

immunoreactive trypsinogen (IRT) and detailed genetic analysis enabling the detection of both novel and less severe mutations. Elevated IRT levels are followed by genetic analysis performed at Stanford University to confirm the presence of CFTR mutations. The analysis uses a "California Panel" of 40 severe mutations representing the most common for the state's ethnic profile. Samples in which only one mutation is identified go through an additional step at Ambry Genetics to identify less common mutations. All infants identified as positive to the screen are referred to CF centers for further evaluation, including sweat testing, to confirm the diagnosis. Based on the data accumulated to date the incidence of CF in the California population is one in 7,014 newborns screened, much lower than the traditional prevalence one in 3,000 births in the overall population.

California CF Centers in collaboration with the Department of Health are following Minimum Guidelines for the evaluation of any newborn that screens positive. Evaluation at the Centers entails sweat testing, further genetic testing, family studies, clinical evaluation and close follow up through the first year of life. After a definitive diagnosis is made, infants are followed at intervals based on clinical status or at a minimum monthly for the first six months of life per CF Foundation (CFF) Clinical Care Guidelines. Phy-

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Our Center's mission is to excel in cystic fibrosis care, to be partners with those we care for, and to be leaders in the discovery process that will produce the cure for cystic fibrosis.

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NEWBORN SCREENING CONTINUED FROM PAGE ONE

sicians at Lucile Packard Children's Hospital are leading a process for all California CF Centers to develop uniform clinical care guidelines for newborns identified by screening, with a goal that infants receive the same care, regardless of geographic location.

First Year of Life

The CF Center team at Packard Children's and Stanford has developed a first-year-of-life clinical model for infants diagnosed through NBS that seeks to set a high standard of preventive care and early, aggressive intervention. The first visit occurs within days of the referral from the Department of Health, typically within the first two months of life. At this visit, confirmatory testing is arranged and initial education is provided to help families understand the newborn screening findings. Within a week of this initial visit, a second visit seeks to establish a "baseline" for each infant with initial lab tests, chest x-ray and physical measures. Packard's multidisciplinary team trains the fam-

ily so that respiratory treatments and nutritional therapy can be initiated while lab results are pending.

Teaching new families about CF is focused on helping them understand the basis of the diagnosis and nutrition including the basic aspects of malabsorption, pancreatic enzyme use and caloric needs. The interdisciplinary team of nursing, social work, respiratory therapy and nutrition play an integral role in the teaching of basic CF care. Visits for new families occur every one to four weeks depending on each family's progress and the infant's medical needs. Most infants are seen monthly for the first six months then every two months until one year of age. At that point, the infant may transition to quarterly visits every three months if they are doing well.

The goal of the Packard Children's/Stanford CF Center NBS Program is to allow every child born with CF to maintain the highest possible level of health through development of strong partnerships with families that facilitate proactive management of the disease. ■

AT 9 MONTHS, A HEALTHY START TO LIFE

Reid Bailey's first nine months are a picture-perfect start to life: an easy home birth, steady growth, healthy appetite and cheerful disposition. The youngest member of the Bailey family brings joy every day to his parents and brother Gregory. His parents, Katherine and David Bailey, hope the early adoption of preventive routines they've learned from the CF team at Packard Children's Hospital will keep them from ever knowing the bad side of CF. They also know that the Packard Children's team shares that commitment to focus on Reid's health, not illness.

When Reid was 7 weeks old, Katherine received a call from his midwife that would forever change the family routines. Four weeks earlier, they had been informed that the Oregon NBS program where Reid's heel stick had been sent found an elevated IRT indicating a possible CF diagnosis. He was referred to the local California hospital for the genetic testing that found two DeltaF508 mutations. Although alarmed, Katherine had followed the story of British Prime Minister Gordon Brown's son's diagnosis with CF with newborn screening when she lived and worked in London. She knew that not every case of CF was severe. One of her first calls was to Packard pediatric CF nurse coordinator, Mary Helmers. Mary assured her that with good and proactive care Reid could live a full and healthy life.



Reid Bailey

The first clinic visit was a blur of new information, people and training. Back in Truckee, the family reconsidered the long drive from the mountains to Palo Alto for regular care and tried a clinic closer to home. But, Packard's caring team, focus on wellness and aggressive treatment brought them back. "The LPCH attitude is, 'we're not going to let Reid get sick,'" says Katherine. "Here is a whole team of specialists ready and anxious to help me raise Reid and keep him well."

The Bailey family believes the CF newborn screening program is the best thing that could have happened to Reid. Now they know what he needs and how to keep him healthy. Katherine cringes at the thought of how many months of angst were prevented by knowing the diagnosis early rather than after Reid got sick. Daily nebulizers and chest physical therapy are a small price to pay for a long life ahead.



Diagnostic Dilemmas Define Research Opportunities

The CF Center at Packard Children's and Stanford has lead numerous research studies in infants with cystic fibrosis diagnosed through newborn screening. Carlos Milla, MD, and Jacquelyn Zirbes, DNP, RN, CPNP, were recruited to Stanford in 2007 and 2008 from the University of Minnesota's renowned CF center to lead the development of a comprehensive clinical and research program for newborns and children with CF. Historically, CF diagnoses were based on elevated sweat chloride test results. The era of genetic screening has introduced greater complexity to the diagnosis and treatment decisions of clinicians and families since some individuals with two mutations present with few, or no symptoms. The uncertain relationship between genotype and phenotype (physical symptoms) creates a significant dilemma.

With grant support from the Cystic Fibrosis Foundation (CFF), the Stanford team is evaluating newborn sweat testing results, fluid and salt balance and whether these factors change over time. They know that how much an infant drinks and his chloride levels may affect sweat testing but this has never been fully determined in newborns. The multi-center study that Milla and Zirbes are leading is assessing whether initial sweat test and genetic testing results can predict changes over time as well as responses to treatment. The study is enrolling 200 children at approximately 15 California CF Centers.

Zirbes and Milla have also instituted a research protocol using an ultrasonic device that measures respiratory flows and lung capacity during regular quiet breathing. A Lung Clearance Index (LCI) is calculated to define the volume of air moving in and out of the lungs. LCI has advantages over conventional infant pulmonary function



Carlos Milla, MD and Jacquelyn Zirbes, DNP, RN, CPNP



testing (PFT) or spirometry since it can be standardized across age groups from early childhood to adulthood, unlike PFTs that vary by age, sex and height. For this reason there is great interest in the CF scientific community in evaluating the utility of these novel measurements. To date, 20 infants have undergone testing with great ease. In those where conventional PFTs were performed; they found that the LCI values compared well to values obtained during conventional PFTs. Further, most of the infants had "normal" PFTs whereas the LCI was found to be abnormal. This provides strong evidence of the greater sensitivity of the LCI test for the detection of early lung disease. There are several advantages to LCI compared to infant PFTs: 1) it is a passive lung measure-

ment that requires some cooperation but no sedation; 2) it is faster and 3) it appears to have a higher sensitivity to the presence of lung disease. Packard's CF team is also involved in ongoing studies to compare early structural changes in the lungs with changes by high resolution CT scans (HRCT).

In general, clinical trials involving infants with CF have been limited. Packard Children's/Stanford is the only site in California participating in a national multi-center randomized trial to assess the use of seven percent hypertonic saline inhaled twice daily for 48 weeks in infants and children 4 to 60 months of age. Investigators propose that hypertonic saline will decrease the rate of pulmonary exacerbations during the treatment period. This study may provide evidence for early use of hypertonic saline to improve mucus clearance and delay or hinder the lung infections and inflammation responsible for progressive airway damage in CF lung disease. ■

Adult CF On the Move

Adult CF Clinic Moves to Stanford Hospital

For the first time in the history of Stanford Hospital and Clinics (SHC), there is a designated Adult CF Clinic. Following months of detailed planning, the new clinic opened November 11, 2009, with two dedicated sessions each week. Located in the Chest Clinic on the second floor of the Boswell Building (in the main hospital building), the new clinic heralds the rapid increase in the number of adults with CF and the recognition of the growing need for pulmonologists and other adult medicine specialists to provide comprehensive care. The clinic continues to gain two to three new adult patients each month, with adult patients now outnumbering pediatric patients 190 to 160. With more than 350 patients, the Stanford/Packard Children's program has grown by almost 50 percent in the past four



Molly Pam

years. The move to SHC will be completed in March 2010 when all adult CF patients will be seen in the new clinic.

The Adult CF Clinic is fully staffed by a multidisciplinary team specializing in adult CF. David Weill, MD, Gundeep Dhillon, MD, Paul Mohabir, MD, and Rama Sista, MD, staff the clinics on Wednesdays and Fridays. They are joined by the inpatient nurse practitioners Camille Washowich, MSN, ACNP, and Erika Rad, RN, MSN, NP, who provide routine follow up and urgent care. Nurse coordinators Kathy Gesley and Nicole Eden moved with the program and are working with the pediatric CF team to orient new team members Leslie Seeger, Social Worker, Carol Power, Respiratory Therapist, and Lara Frett, Registered Dietitian as well as other clinic staff.

The pediatric CF team continues to closely collaborate with the adult team in care management, research, weekly case conferences and consultations. The CF research coordinators attend all clinics to recruit new clinical trial participants.

Diabetes Clinics Added

A major benefit of the new clinic will be realization of the team's quest to develop a joint diabetes clinic with adult endocrinologists. Tracy McLaughlin, MD, and Marina Basina, MD, will begin scheduling patients in the Chest Clinic during CF sessions approximately twice a month starting this spring. They are joined by diabetes educator Anna Simos. Basina worked with adult CF patients at Kaiser before coming to Stanford. The new joint clinic will provide adults with both diabetes and CF access to a high level of care coordination that isn't available in most CF clinics across the country. Visits can be scheduled through the Chest Clinic/Adult CF Clinic at (650) 497-8510.

A New Era for Adults with CF

The move to SHC marks a new commitment to adults with CF by the Stanford medical community, a commitment made possible with growth of the program, effective physician leadership in both the pediatric and adult CF and pulmonary programs, and the advocacy and support of adults with CF and their families. A modest endowment fund was established in 2007 to help support the program. All members of the team aspire to ongoing program improvements. Dr. Weill is committed to further development of the program and hopes to continue to work with the community in this endeavor.

Inpatient Adult CF Unit Moves

"New space, same staff" sums up the relocation of the adult CF inpatient service to the third floor of Stanford Hospital. Rudy Arthofer, RN, patient care manager of the unit, explains the move as an expansion of services to enhance continuity of care for adults with CF. The unit staff is paired with the intermediate intensive care unit located next door. Arthofer notes that as the patient population has grown so has the demand for higher levels of care. He sees the move as a huge statement of Stanford Hospital's long term commitment to the CF program.

Christine Thompson, RN, BSN, CNS, is the new clinical nurse specialist charged with educating staff about CF.



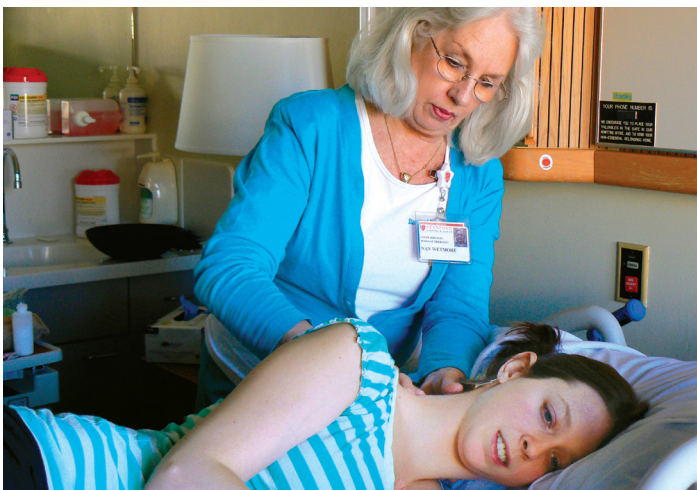
She rounds with the CF team and reviews charts to provide feedback on standards of care. Infection control is a primary concern. Arthofer observes that the typical adult with CF is much more knowledgeable about their disease and treatment options than other inpatients, a characteristic that can lead to successful provider-patient experience. The nursing staff is committed to offering personalized care as they get to know more patients and gain experience with a broad spectrum of CF-related conditions.

One service that didn't change when the unit moved is access to Stanford's expert massage therapy team. An anonymous donor made it possible for adults with CF to receive up to two free massages a week in the hospital. Professional masseuses who specialize in working with hospitalized patients provide this unique service, working with patients upon request. A half-hour massage delivered by gentle hands eases the stress of hospitalization.

Not Your Typical Hospital Food

Stanford Hospital has teamed up with chef Jesse Cool to reinvent hospital food: Farm Fresh with Jesse Cool. A menu of fresh organic and locally grown ingredients offers items such as corn with basil and smoked cheddar soup, whole grain breads and seasonal local fruit with honey yogurt sauce. The menus are served with organic tea, lemonade, milk and locally grown salads. Cool reminds visitors that "100 years ago, visitors could see acres of carrots, corn, barley, alfalfa, orchard and vineyards planted by Jane and Leland Stanford, affectionately known as "the Farm." Stanford takes pride in honoring this heritage with a new approach to hospital food." Jesse Cool, chef at Flea Street Café and the Cantor Center café, is passionately committed to flavorful and sustainable cuisine.

Molly Pam and massage Therapist Nan Wetmore



Jesse Cool

"Buying locally provides great quality, boosts the local economy, protects farmlands and keeps people and the environment healthy."

CF Research Team Updates for Adults

As the adult program transitions to Stanford, the research team wants to provide you with some important updates:

1. The research team will remain the same across both the pediatric and adult programs.
2. One of the research coordinators will be in all clinics to answer questions and recruit new study participants.
3. The team will continue to have a collaborative program between the pediatric and adult physicians.
4. The pediatric and adult physicians will continue to be principal investigators and sub-investigators on all trials.
5. All pediatric physicians, adult physicians, clinic nurses and the research team will continue to meet monthly to discuss current studies and all upcoming projects.
6. For more information about research please contact Colleen Dunn at (650) 736-0388 or Zoe Davies at (650) 498-5315.

STAR Survey on Clinical Trial Participation

The Stanford CF Research Team is conducting a survey of all past and present research study participants in order to improve the overall quality of our research program and to identify potential barriers to research participation. If you or your child has ever been involved in a study at Packard Children's or Stanford you can expect to be approached by Cathy Hernandez (our database coordinator), and asked approximately 30 questions pertaining to your research experience. Staff will then analyze the data and opinions gathered, submit an abstract to the national CF conference in October 2010, and implement any necessary changes. We thank you in advance for taking the time to contribute to this important project. ■

Stanford Cystic Fibrosis Discovery Series



Camille Washowich, MSN, ACNP, and John Mark, MD, with Carroll Jenkins, CFRI Executive Director (l to r)

Adult CF nurse practitioner Camille Washowich, MSN, ACNP and Carroll Jenkins, CFRI Executive Director, have developed a patient education series focused on living longer and healthier lives. More adults with CF are enjoying family and careers, requiring them to cope with stresses rarely imagined in previous generations. Multitasking life on top of managing a complicated disease can be overwhelming. Patients often ask for help in managing daily life with CF, hence the new program.

The “Stanford Cystic Fibrosis Discovery Series” name was chosen by an adult with CF who said that discovering for one’s self was much more meaningful than hearing a lecture. He also believed that the best work could be done by people with CF helping each other. The program is working to create a CF community similar to past years before isolation protocols were introduced. The series is open to adults with CF, families and friends. Videotapes are available at the hospital as well. The cost with parking is free. Classes are held at the Crowne Plaza Hotel in Palo Alto.

The first programs dealt with compliance, the healing power of humor, supporting caregivers, stress management, depression, dating, marriage and fertility. Stanford staff, faculty, CF caregivers and other professionals in the community lead the programs that include:

- March 9, 2010 Lung Transplantation: Discussing Lung Transplantation
- April 13, 2010 Exercising Your Options: Creative Ways to Exercise and Do Lung Treatments
- May 11, 2010 Actualizing Our Dreams and Discovery Through the Power Within: Enhancing the Quality of Your Life ■

Adult CF Patient and Family Advisory Council Launched

A new advisory council is working with the adult CF team and Stanford Hospital & Clinics (SHC) staff to improve patient services as the program moves to SHC. Chaired by Norma Kipp, the council is seeking new members, particularly adults with CF.

The Council seeks members who are inspired to participate in and contribute to ongoing efforts to improve the quality of CF care at SHC. It explores and addresses issues that impact every aspect of the CF patient experience. The council includes current patients, family members, community friends, and medical professionals who work closely with SHC physicians and staff offering ideas, perspectives and recommendations with the goal of helping the organization to better understand and improve patient care. Applications are available online at <http://cfcenter.stanford.edu>. ■

MISSION STATEMENT

The Cystic Fibrosis Adult Patient and Family Advisory Council provides feedback to and partners with members of the Stanford health care team to improve the patient and family experience at Stanford Hospital & Clinics (SHC). The Advisory Council is committed to excellence in the entire adult cystic fibrosis experience at SHC, including pediatric transitional care from Lucile Packard Children's Hospital to adult care at SHC.



Nutrition: the Foundation of Good Health

California's newborn screening program provides an important opportunity for infants with CF. Studies have found improved growth and nutrition in regions where NBS is routine. Optimal growth is correlated with higher lung function in CF. The Packard Children's team follows newly established national guidelines to ensure close monitoring of growth and nutrition of newborn infants with CF.

In the first year of life, it is recommended that infants achieve a weight gain of 35 grams per day with a caloric intake 110 percent to 120 percent greater than infants without CF. Packard's CF team helps families achieve these goals by teaching ways to monitor intake and concentrating breast milk or formula when necessary. It is also important that infants with CF receive enough salt, estimated at 1/8 to 1/4 teaspoon daily until high salt foods become a part of a toddler's diet, usually around age two.

Fat soluble vitamin supplementation (A, D, E and K) is recommended for all newborns with CF within the first few weeks of life. Infants with pancreatic insufficiency can develop vitamin A and E deficiencies very early, with

significant effect on growth, development and immune function. Most clinics, including Packard Children's, begin pancreatic enzymes before pancreatic sufficiency is confirmed if an infant has GI symptoms or genetic mutations typically associated with insufficiency. Stool samples are sent to the lab to determine if there is enough of the enzyme elastase for a functioning pancreas. Enzymes and vitamins may be discontinued if the tests do not show a deficiency.

As infants become toddlers, children, adolescents and adults, it is the objective of the Packard Children's team to closely monitor the nutritional status of all patients. A comprehensive nutrition review is an important part of each clinic visit to provide the best opportunities for optimal growth and lung function and to support an active and full life for our patients. ■



IN THE NEWS



Rick Moss, MD, who has led the CF Center from 1991, will be retiring in March. Moss will continue as an active Emeritus Professor seeing patients in clinic and overseeing a number of research projects for the CF Center. **Carlos Milla, MD**, has assumed overall leadership as Center Director. Moss chaired a session and spoke at the 4th

international Advances Against Aspergillosis meeting in Rome in February.

Bruce Reitz, MD, who led the Stanford heart and lung transplant team for more than 20 years, is also retiring in March.

Cathy Hernandez joined the CF research team in April 2009 after working in the CF clinic and the Pediatric Pulmonary Division. She has worked at Stanford for 18 years. She manages the CF Patient Registry as a database and patient consent specialist. Cathy says, "I have always been interested in learning more about CF and helping in research to find a cure. I am really enjoying this new venture and can't wait to see what the future holds."



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CURRENT RESEARCH STUDIES

Be a part of the cure for CF! Volunteer for a clinical trial today. To learn more, visit <http://cfcenter.stanford.edu>, contact our research coordinators or talk to your physician. The following trials are currently underway:

- Phase 3 denufisol "Tiger 2" extension study
- NAC Phase IIb
- Pulmonary Exacerbation
- Sweat testing in newborns with CF
- Chest CT and natural history of CF Lung disease
- Phase III study of VX-770 (for G551D)
- Phase II study of VX-809 (for Delta F508)
- Phase II study of GSK oral anti-inflammatory (enrolling)
- Phase II study of inhaled fosfomycin-tobramycin (FTI)
- Exercise study
- Omalizumab for ABPA study
- EPIC trial for early treatment of Pseudomonas
- Lung Clearance Index
- ISIS – Infant inhaled saline study
- PTC124 Phase III (for stop mutations eg G542X)

Visit our Web site at
<http://cfcenter.stanford.edu> for more
information about our center and CF.

CYSTIC FIBROSIS CENTER AT STANFORD

Pediatric Providers: Carlos Milla, MD, Center Director; Carol Conrad, MD; David Cornfield, MD; John Mark, MD; Richard Moss, MD; Terry Robinson, MD; Lauren Witcoff, MD; Nanci Yuan, MD; Jacquelyn Zirbes, DNP, RN, CPNP.

Adult Providers: David Weill, MD, Adult Program Director; Paul Mohabir, MD; Gundeep Dhillon, MD; Rama Sista, MD; Camille Washowich, MSN, ACNP; Erika Rad, RN, MSN, MP

Clinic Scheduling – Pediatrics	(650) 497-8841
Clinic Scheduling – Adults	(650) 497-8510
Clinic and Prescription Refill FAX, Pediatrics	(650) 497-8837
Clinic and Prescription Refill FAX, Adults	(650) 723-3106
Miguel Huerta, Patient Services Coordinator (Peds)	(650) 498-2655
Mary Helmers, Pediatric Coordinator	(650) 736-1359
Kathy Gesley and Nicole Eden, Adult Coordinators	(650) 736-1358
Jacquelyn Zirbes, Newborn Screening Coordinator	(650) 721-1132
Kristin Shelton, Pediatric Respiratory Therapist	(650) 724-0206
Carol Power, Adult Respiratory Therapist	(650) 736-8892
Julie Matel, Pediatric Nutritionist, Dietician	(650) 736-2128
Lara Frett, Adult CF Registered Dietician	(650) 721-6666
Lindsey Evans, Pediatric Social Work	(650) 736-1905
Leslie Seeger, Adult CF Social Work	(650) 723-6273
Colleen Dunn & Zoe Davies, Research Coordinators	(650) 736-0388

For Urgent Issues:

Monday-Friday 8:30 am-5 pm, contact RN Coordinator.

All other times, for children call (650) 497-8000 and for adults call (650) 723-4000 and ask for pulmonary physician on-call.

Visit our Web site at <http://cfcenter.stanford.edu> for more information about our center and CF.

To subscribe to this newsletter please contact Cathy Hernandez by phone at (650) 724-3474 or by email at cathyh1@stanford.edu.

We gratefully acknowledge the leadership of friend and parent Penny Stroud in producing this publication.