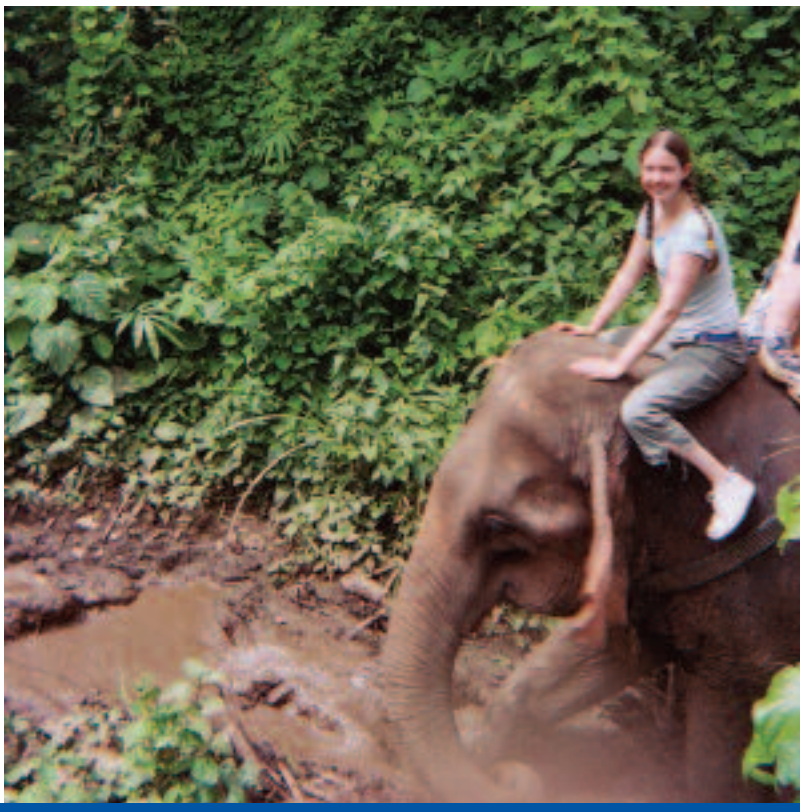
Lucile Packard Children's Hospital AT STANFORD

CYSTIC FIBROSIS CENTER NEWS

Exploring the World with CF



Sixteen year old Molly Pam met her dance group in Thailand this summer for 8 days of a 21-day trip.

Remote beaches. Elephant rides in the jungle. Venetian sunsets. School trips with friends to far-off places. Who doesn't harbor dreams of an escape from the rat race? Add CF, and the dream seems impossible. Yet, with proper planning, flexibility and realistic expectations, long distance travel is possible—and rewarding—even with CF.

Choosing a Destination

Health is the first consideration in traveling with CF. Starting off in good health often requires planning—talk to your doctor and the nurse coordinator, and research your destination and itinerary. If doing well before a trip, ask if some treatments may be skipped or reduced; the location and timing may determine what you take and how you manage treatments. Flexibility is important since you can't know if you will be healthy when it's time to go. Trip insurance and refundable tickets, often inexpensive if purchased when you buy your tickets, can mitigate the financial risk of last minute changes. Frequent flyer miles are also extremely flexible.

Research your destination and arrangements as you plan. Travel forums on the web, the Centers for Disease Control (CDC) website, travel agents specializing in an area, and acquaintances are good sources of information. 16-year old Molly Pam's family cancelled plans to travel to Bali last summer due to SARS, but successfully spent two weeks there, and one in Thailand, this year. The CDC website lists travel advisories and immunization recommendations. The web allows you to communicate with hotels and local guides about such things as transportation, refrigeration and local sanitation. Consider your tolerance for heat, activity and food before finalizing plans. Staying longer in one place is easier than moving around. Taking time out to adjust to time zones and planning days around needed treatments, help to pace a trip. Trying to fit in too much can ruin a trip if your health is compromised. Better to relax, enjoy less ambitious activities and start each day rested. Recognize signs of exhaustion and slow down.

After saying "no" to a school-sponsored trip to China, and canceling a trip last summer, the Stroud-Pams met Molly's dance troupe in Thailand. Molly participated in a dance exchange and other activities, but was able to return to the hotel to swim, cool down, rest and do her medications. (This compromise also left her convinced that the dawn-to-dusk itinerary planned by the school was too demanding!) In Bali, daily dance lessons were a unique experience, and curbed the drive "to do it all". Staying in one place for two weeks limited the scope of travel, but provided an incredible opportunity to get to know one area. Renting a house or apartment in the countryside or a foreign city can provide a "home base" that helps to manage treatments and activities.

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OUR COMMITMENT TO AGE APPROPRIATE CF CARE

A commitment to excellence across the spectrum of age and disease is our goal at the Stanford CF Center. A dedicated, multidisciplinary team of caregivers is the hallmark of our program. As many of you are aware, Noreen Henig, Adult CF Center Director of the past five years has resigned her position. We want all of our patients to know that we, the CF team, LPCH and Stanford Hospitals and the School of Medicine, are committed to the maintenance and ongoing development of an outstanding adult CF center program. Judy Swain, chair of the Department of Medicine, states, "I agree that this is a critical program, and I and the pulmonary leadership started working on this issue in July."

Drs. Steve Ruoss and Glenn Rosen, the co-chiefs of Adult Pulmonary/Critical Care, in concert with the CF Center physicians, have developed an interim plan to assure that care of adults with CF continues without interruption. Dr. Rosen said, "Continuity of care is critical and our first priority. We all agree that it is best if the pediatric pulmonary team care for our adults during the transition because of their experience with CF. Together, Stanford Hospital, LPCH, the pediatric and adult pulmonary divisions and the Department of Medicine are working toward a permanent solution as quickly as possible. The pediatric CF Center physicians have cared for adults for years, and the remainder of the CF care team is intact. They have routinely helped in the management of inpatient care, and have provided care when the adult CF physicians were unavailable. This transition also provides the opportunity to enhance the quality and integration of the adult and pediatric programs."

Adult CF Nurse Coordinator Mary Helmers, R.N. will continue in her pivotal role, with assistance from Nicole Eden. Mary has been a committed member of the CF team for many years (see following story). She notes, "Our adult patients should be assured that very little is changing. The pediatric physicians always have been part of the adult CF care team, and they know most of the patients already." CF Center physicians Richard Moss, Terry Robinson, Carol Conrad, Laurie Witcoff and Nanci Yuan will each care for a group of adults until a new director is recruited.

Nancy Lee, Vice President of Stanford Hospital, states, "Stanford Hospital and Clinics is committed to support the Cystic Fibrosis Center both now and in the future. We believe that people with CF are best cared for in a program that spans the transition between childhood and adult care. We are actively working with the Department of Medicine to ensure that our program remains one of the best centers in the country."

The Department of Pulmonary/Critical Care Medicine has initiated recruitment efforts, and a search committee has been appointed. We will be recruiting the best possible physician to fill this important position and expect to maintain the high standards that have distinguished both our adult and pediatric programs.

Stanford/LPCH CF Team
Front Row (left to right): Miguel Huerta, Rick Moss, MD, Kristin Shelton, RPT, Noreen Henig, MD, Lauren Witcoff, MD, Carol Conrad, MD, Terry Robinson, MD, Chandra Mcduffie. Top Row (left to right): Leticia Alcantara, Mary Helmers, RN, Deb Robinson, RN, Katherine Boyle, RN, Violet Hsieh, RD, Monica Smith, RN. Not shown: Nanci Yuan, MD and Julie Matel, RD.

CFRI Award Recognizes Helmers' Commitment to CF

"As long as I work with CF, I'm happy." For patients and colleagues, the feeling is mutual. Mary Helmers' commitment to CF defines her 20 years at Stanford. She joined the CF team in 1992. four years ago she was named the first adult CF nurse coordinator, helping to build one of the largest adult centers in the country. That move keeps her in touch with patients and friends she's known since they were children.

In August, Cystic Fibrosis Research, Inc. recognized her with the 2004 Professional of the Year Award. Her nomination stated, "Mary is the most dedicated professional with whom I ever have worked. She is the backbone of the program. Her attention to detail, warm personality, and boundless energy has benefited hundreds of patients over the years. Although I could fill a small book with lists of Mary's talents, I would like to highlight one. Mary sees patients as individuals first and foremost. She recalls the important events of our patients' lives and incorporates it into their care. She will remember an anniversary, a fear expressed, an upcoming graduation, or a wish fulfilled. It is often these bits of information that make a HUGE difference in the care of individuals with CF."

Reflecting on her work, Mary states, "I don't look at them as patients with CF, I look at them as peers—people like me with careers, families and a life to manage. Being able to talk and give "life advice" is what I enjoy. Adults with CF are amazing, with all they do and accomplish."

Helmer's tenure with the CF program means she knows each patient's needs, "There's an advantage to that and knowing the system. I can be an effective patient advocate when talking to doctors and developing care plans. The patient always comes first." Her relationships with the team and her patients are built on a foundation of mutual trust, security and respect. Her philosophy, which she says is shared by all members of the CF team, is to treat patients the way she would want to be treated.

"I don't look at them as patients with CF, I look at them as peers—people like me with careers, families and a life to manage. Being able to talk and give "life advice" is what I enjoy. Adults with CF are amazing, with all they do and accomplish."

MARY HELMERS, RN
Adult CF Nurse
Coordinator

Mary values the multidisciplinary Stanford CF team and the hospitals' commitment to excellence. Most of the team has enjoyed working together for years, a strong factor in her job satisfaction. The integrated adult and pediatric program allows collaboration and continuity of care. Mary also thinks that adults with CF offer hope and teaching opportunities for younger persons with CF and their families. She has been integral in working with team members to develop programs such as CF mentoring and transition of teens to adult care. Job-sharing with former pediatric coordinator Nicole Eden, and Mary's former role as pediatric coordinator, provides further opportunities for continuity and communication in the clinic. Dr. Moss states, "Mary is the hub of the wheel that unites all the different components of complex adult CF care. No one does it better, period."

Mary's commitment to family mirrors her commitment to the job. Matthew (10), John (7), husband Tom and her extended family, help to balance baseball games and schoolwork. Exercise, cooking and spending time with family keep her busy when she's not at Stanford. Mary, like her patients, appreciates the opportunity to be her "day to day normal self."

Bench to Bedside Research: Wine's Lab Ties Mucus Defects to CF Treatments

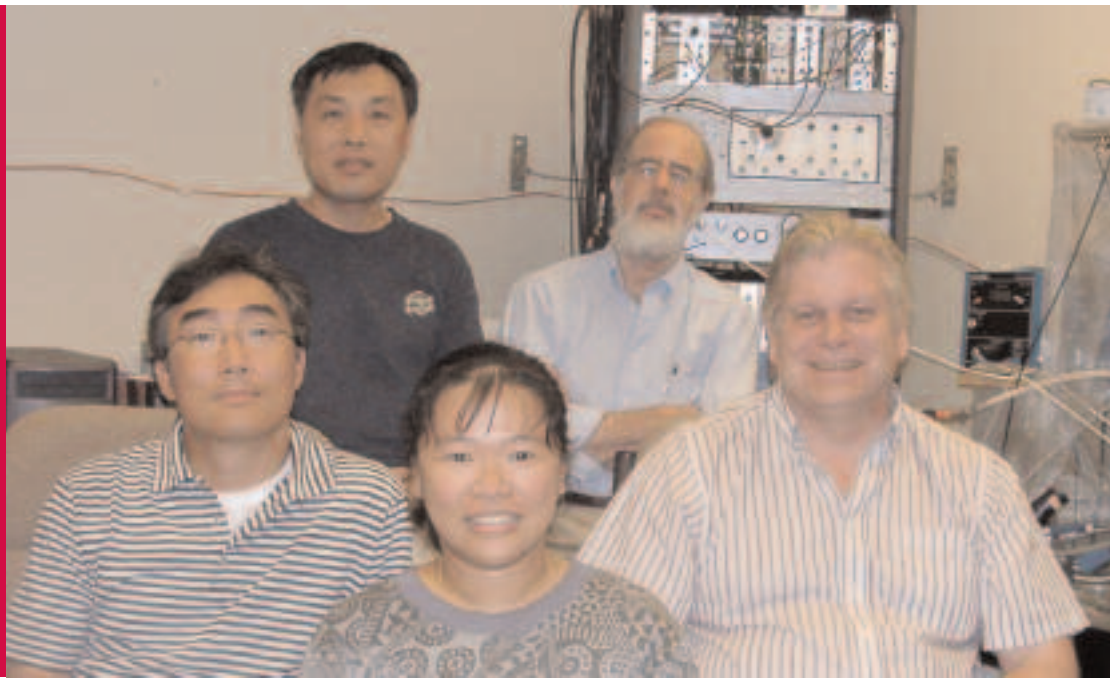
Why do people with CF harbor chronic lung infections with bacteria that are harmless for most people? For years, scientists attributed it to overproduction of thick, sticky mucus that couldn't be cleared properly from the airways. Jeff Wine's CF Research Laboratory at Stanford is finding that explanation to be only partly true, with much more than that to the story.

About 95% of the mucus in normal airways comes from tiny glands beneath the surface of the airways. A patch of airway the size of a postage stamp has 500-1000 glands under its surface, and each of these miniature organs uses at least four types of cells to produce the mucus that coats the airways. Normal mucus is comprised of water, salt, and proteins that protect the airways and help to expel foreign substances such as bacteria, allergens, and dust. People with CF think of mucus as a nasty side-effect of their disease, but what you cough up is actually only partly mucus—mostly it is a mixture of bacteria, sometimes fungus, and countless dead and disintegrating white blood cells.

Wine's lab studies the mucus produced by glands from people with and without CF. Glands are obtained from lungs taken out during transplants, and from unused portions of the lung donors' tracheas. After the infected mucus is cleared away from CF airways, these glands produce mucus that looks superficially like normal mucus. The mucus secretions are studied by covering clean airways with oil, into which the glands secrete bubbles of mucus. CF mucus is a colorless semi-gel, and like normal mucus it is moved out of the airways by mucociliary clearance, although at a slower rate. Also like normal mucus, it contains hundreds of different proteins designed to make life miserable for bacteria. Some proteins trap the bacteria so the mucus flow can carry them out of the airways; others are natural antibiotics that kill bacteria or inhibit their growth.

Why don't bacteria develop resistance to these natural antibiotics? First, bacteria don't have time in a normal lung, because they are quickly swept away by mucus clearance. But another reason is that natural airway antimicrobials kill bacteria in so many different ways that no bacteria can evolve defenses against all of them. For example, Wine's lab recently found that mucus gland cells release a protein called siderocalin; others have shown that this protein binds to iron atoms after bacteria have specifically tagged the iron for their use. This trick makes siderocalin more efficient than lactoferrin, another mucus protein that competes with bacteria to bind any iron.

If CF mucus has the same rich array of antimicrobials as normal mucus, what is wrong in CF? Wine's lab recently demonstrated that mucus secreted by CF glands does not respond to some kinds of stimuli and has half the normal response to other kinds of stimuli. In contrast to long-held beliefs, they discovered that CF glands do not secrete too much mucus as a basic defect, but rather *too little*. The reason people with CF have so much mucus is that infections and inflammation stimulate secretion and also induce a huge



Jeff Wine (right, upper)
Jin Wu (left, upper)
Mauri Krause (right, lower)
Nam Soo Joo (left, lower)
Wei Chen (central, lower)

movement of white blood cells into the airways. Pure CF mucus *is* thicker than normal mucus, which causes it to get stuck within the glands ducts before it reaches the airways. Wine hypothesizes that CF mucus sometimes becomes "tethered" to the mucus gland ducts where it may persist in the airways for weeks or months, during which time its natural antibiotics are used up and it becomes a medium for bacterial growth. He also hypothesizes, based on experiments in CF mouse intestine, that the natural antibiotics in CF mucus are not properly dissolved, and hence are much less effective than in normal mucus.

Glands are only one part of the story. The surface of the airways normally secretes a thin watery layer of fluid that lubricates mucus flow. This is deficient in CF because too little water is secreted and too much is absorbed, further contributing to thick sticky mucus.

These combined defects make CF mucus less effective at killing bacteria both directly and by mucus clearance. But, just as natural pancreatic enzymes can be supplemented with encapsulated enzymes, so can the natural defenses of CF airways be supplemented with inhaled antibiotics and vigorous physical therapy to augment the weakened antimicrobial properties and sluggish mucus clearance of CF lungs. Wine speculates that if these methods were to be applied rigorously before airway infections become established, that is, shortly after birth and daily forever after, it is possible that CF lung disease could be held at bay for at least several decades, and maybe permanently. Clinicians, however, worry that early and ongoing use of inhaled antibiotics could lead to emergence of intrinsically resistant and more difficult-to-treat bacterial infections. The team of basic and clinical research scientists, Wine's lab, the CF Foundation and Stanford's CF team are working to test new—and old—treatments to determine the most effective ways to improve CF clinical care. New—and old—treatments are being tested to identify more effective protocols for clinical care.

Living human submucosal gland.

Father & Daughter: Jeff & Nina Wine

JEFF WINE: CF PARENT & SCIENTIST

Jeff Wine, Director of the Cystic Fibrosis Research Laboratory at Stanford, came to Stanford 30 years ago as an assistant professor of psychology. In 1981, doctors diagnosed his first daughter Nina with CF, forever changing his personal and professional life. Moving from the science of neurons to the function of CFTR in ion channels marked a change in focus that led to 30 years of contributions to understanding the basic defect in CF. His collaborations with the basic scientists and clinical teams who study aspects of CF at Stanford, and across the country, have been pivotal in developing a team committed to understanding CF. "We don't have a building dedicated to CF research at Stanford, but we do have an effective network of researchers pursuing the problem—and biology teaches us that networks are efficient ways to accomplish complex tasks," Wine states. Jeff has also mentored students and fellows who go on to become dedicated CF clinicians and scientists. He contributes time and energy to local, regional and national CF clinical and scientific forums, including many years of service on the CF Foundation's advisory committees. He is also Director of Stanford's undergraduate program in Human Biology.

Exploring the World with CF

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Pre-trip Planning

A trip with CF requires organizing drugs, equipment and supplies. Airway clearance can be managed manually, or with swimming. In the U.S. the Vest can be checked as baggage (call the airline to ask for a weight/excess baggage exception), or sometimes one can be rented at your destination. Other things to consider:

Air Compressors: Several small ones are available with batteries, car converters and voltage adapters. The new Pari Trek is almost pocket-sized, and runs +/-90 minutes on rechargeable batteries. The small ultrasonic compressors are not recommended for most CF medications.

Nebulizers: Take enough for several days, and bring containers for washing (plastic ice cream containers work well!). Liquid soap and liquid bleach are easily available for sterilization. Paper towels and disinfectant wipes keep things clean while mixing and drying.

Hand Cleaner: Gel hand cleaner in pocket-sized containers is invaluable for fixing nebs, and before/after eating, sightseeing and using the restroom.

Medications: Bring original bottles and prescriptions to verify with authorities, or for refills. Bringing enough meds, as well as having contingency meds, can save time and money (e.g. for diarrhea, GoLytely for constipation, Vitamin K for hemoptysis, diabetic supplies). Bring a letter from your doctor explaining CF and listing meds and equipment. Drafting the letter and having it available electronically helps the CF center respond on a timely basis. Identifying local health providers is useful for emergencies, or if things don't go as planned. Check the web or ask your CF Center about resources at your destination.

Other supplies: salt tablets, electrical plug adapters, and other supplies may be needed, depending on the venue.

Double check a list of needed supplies as you pack; some can be difficult to find in remote places. The CF Center has a comprehensive list of travel tips to help in your planning.

In the Air

Hand carry medications, nebulizers and your air compressor in case luggage is lost. A portable compressor can be used at the airport or while touring. A mask may prevent airborne illnesses in airplanes and cities with polluted air. Saline spray can help if the dry air of planes is bothersome. Extra water helps to prevent dehydration. Some people need extra oxygen while flying (check with your doctor if lung function is low). Keep Pulmozyme cold in an insulated bag. TOBI can be left at room temperature for up to 30 days.

Pace Yourself and Relax!

Getting enough sleep, eating well and planning activities according to your energy are critical to a successful trip. Travel can be stressful if everyone has a different agenda, so discuss expectations and plans before you go. Splitting up for some activities may seem unfair, but an ice cream store around the corner, a park or even the hotel pool, can offer as many new experiences as a hike or long day on a hot tour.

Risks & Rewards

Traveling is not without risk. Understanding and anticipating potential adverse events, and thinking about how you would manage in an unfamiliar place, help to plan a trip with realistic boundaries, and immeasurable rewards. A successful trip can provide a break and a sense of normalcy and independence. Finding the right place takes organization, but the memories can last a lifetime.

GO FOR THE GOLD: CFF NATIONAL WEBCAST FEATURES LPCH

The CFF fourth Virtual Patient Education featured the Stanford CF team on September 21. More than 600 participants from around the country joined the live webcast to learn more about achieving excellence in the clinical care of CF patients. Dr. Moss, respiratory therapist Kristin Shelton and nurse coordinator Mary Helmers provided an overview of the CFF Clinical Care Guidelines and fielded more than 40 questions from the audience. An archive of the webcast, and other virtual patient education programs can be viewed at **www.cff.org.**

STANFORD IN THE NEWS

CF team members Julie Matel, Kristin Shelton, Joanne Asano, Mary Helmers, Katherine Boyle, Nicole Eden, Gail Farmer, Judy Kirby and Penny Stroud presented a poster on "Tools to Improve Adherence to CFF Guidelines" at the NACFC conference in St. Louis in October. Drs. Moss, Robinson and Conrad participated in panel discussions and presentations on imaging, transplant, gene therapy and clinical trials at the meeting.

Dr. Moss was joined by Dean of Stanford Medical School Philip Pizzo and Stanford infectious disease expert David Stevens as faculty at an international conference on aspergillus held in San Francisco in September. The conference was organized by Stevens, Moss and others. Dr. Moss discusses asthma treatment on the web at http://www.healthtalk.com/asthma/askthedoctor/index.cfm. His other recent activities have included presentations at a CFF meeting on gene therapy in September, assistance in development of a CF Standards of Care tool for insurance companies to improve reimbursement for CF care; contributions to new educational modules sponsored by Genentech; and a collaborative study on the effect of parental stress on adherence led by Brazilian psychiatrist Ivan Figueria.

Lauren Witcoff gave Pediatric Grand Rounds at Salinas Valley Memorial Hospital on "Chronic Bronchitis in Children" in July.

Terry Robinson published a review of CF-related computerized tomographic imaging research entitled, "High Resolution CT Scanning: Potential Outcome Measure" in the November issue of Current Opinions in Pulmonary Medicine. He and Dr. Moss co-authored "Quantitative Air Trapping Analysis in Children with Mild Cystic Fibrosis Lung Disease" in the November issue of Pediatric Pulmonology.

FLU SHOT REMINDER

Be sure to schedule an annual flu shot this fall. Shots should be available in October, either through your primary care doctor, a community clinic or the CF Clinic. If you get the flu, prompt treatment is important to minimize complications. Be sure and get plenty of rest and drink lots of liquids. Also, if taken within 24 hours of symptom onset, prescription medications are available that sometimes mitigate severity. Call the nurse coordinator or, if on a weekend, the physician on-call, for more information.

CURRENT RESEARCH STUDIES

Help find the cure for CF by participating in a clinical trial! Visit www.cfcenter.stanford.edu or contact our research coordinators to learn more. Current trials include:

- Phase IIB AAV-CFTR gene therapy 25E01
- CF.Doc internet-based clinical care (up to age 21)
- Infant and toddler pulmonary testing (4 months to 2 years)
- CF Diabetes
- Induced Sputum: evaluation of anti-inflammatory agents
- Altus TheraCLEC new pancreatic enzyme Phase II
- Effect of stomach acid suppression on gut bacteria
- Oral glutathione precursor (NAC) study

Studies recently completed: BIIL 284.45, Dry Tobi Powder, Aztreonam for inhalation

Upcoming studies: Early Pseudomonas intervention, longitudinal chest CT scans, Tobi Dry Powder Phase III, Inhaled Aztreonam Phase III, PTC124 for stop mutations

EPIC STUDY TO ASSESS EARLY PSEUDOMONAS TREATMENTS

Two new studies sponsored by the CFF Therapeutics Development Network will evaluate the risk factors and treatment impact of Pseudomonas aeruginosa (PA) acquisition and early treatment in children with CF. Site investigator Rick Moss says this large, nationwide long-term study should help determine the best treatment for first acquisition of PA. The two linked studies will compare antimicrobial therapy for new onset PA infection. For the observational arm of the study, 1,400 enrollees will be followed, of which an estimated 650 will likely acquire and be treated for PA during the 5-year term of the study. 300 enrollees will be sought for a concomitant study on the efficacy and safety of treatment with one of two early PA antimicrobial protocols at the time of first positive culture for PA.

CF CLINIC MOVES TO NEW BUILDING

The CF Clinic is moving across the street to 730 Welch Road—directly across from the LPCH entrance. The new clinic should improve efficiency with an increased number of treatment rooms, more parking (and it will be free!), and new technology to speed registration and coordination of care. The pulmonary and CF clinic will be located on the first floor. The move, which is planned for mid October, is part of Phase I of the LPCH facility expansion that will conclude in 2006 with the following:

- Mary L. Johnson Pediatric Ambulatory Care Center
- New medical records area
- Heart Center
- Dialysis center
- Cancer Center
- Six pediatric operating rooms
- Expansion of intensive care

Phase I will increase capacity for beds, surgery, diagnostic services, outpatient and support services. The new clinic will have satellite radiology, a lab drawing station and clinic spirometry. The pulmonary function lab will move to Clinic E, with the Cardiology & Oncology Clinics. In the next phase, the pft lab will move to the new Heart Center.

Most registration will be done by ACC staff over the phone and verified at check-in. There will be a registration desk in the new lobby for the Lab and Radiology services in the clinic (CT, MRI and certain other imaging services will remain in the hospital). Patients having diagnostic testing other than Lab and Radiology will still register at the LPCH Admitting Office, however the volume of patients and waiting time should be significantly reduced. Parking also should improve for both clinic outpatients and hospital inpatients and visitors.

SAVE THE DATE! CF EDUCATION DAY 2005
SATURDAY, MARCH 12, 9-3 pm

VISIT WWW.LPCH.ORG TO SEE THE STENZEL TWINS & CF FEATURED ON LPCH'S WEBSITE HOME PAGE

OPEN ENROLLMENT REMINDER

Be sure to select a health plan that accepts Stanford physicians and hospitals if you have open enrollment this fall. Go to www.lpch.org or www.stanfordhospital.com for details on which plans will be accepted in 2005.
If you change insurance plans, please call or fax the CF Clinic with your new membership information prior to your next appointment so that we can facilitate authorizations and approvals.

CYSTIC FIBROSIS CENTER AT STANFORD

Center Physicians: Richard Moss, Director; Carol Conrad, Terry Robinson, Lauren Witcoff, Nanci Yuan

Clinic E Scheduling	650-497-8841
Clinic Fax	650-497-8837
Katherine Boyle, RN Pediatric Coordinator	650-736-1359
Mary Helmers, RN Adult Coordinator	650-736-1358
Kristin Shelton, Respiratory Coordinator	650-724-0206
Julie Matel, Nutritionist, Dietitian	650-736-2128
Joanne Asano, Social Work	650-736-1905
Research Coordinators	650-736-0388

For Urgent Issues:
Monday–Friday 8:30-5:00 pm contact RN Coordinator
All Other Times (ask for Pulmonary Physician On-Call)
650-497-8000

See our website at http://cfcenter.stanford.edu for more information about our center, CF and current topics.

To subscribe to this newsletter please call or email Judy Kirby at 650-724-3474 or jkirby@stanford.edu

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

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