Chronic pulmonary disease is one of the main characteristics of cystic fibrosis (CF) disease. It is caused by chronic bacterial infection and inflammation in the airways of patients with CF. Development of new or changes in respiratory symptoms and signs are termed "pulmonary exacerbation." Pulmonary exacerbations are associated with worse quality of life and a shorter life span. Therefore, these episodes need to be recognized early and treated aggressively in order to relieve symptoms and maintain pulmonary function.

What is a pulmonary exacerbation? A pulmonary exacerbation is an acute worsening of a patient’s pulmonary CF disease. Development of new general and respiratory symptoms or the worsening of existing symptoms can be consistent with a pulmonary exacerbation. There are multiple symptoms, signs, and diagnostic tests that can indicate a pulmonary exacerbation. Among expert providers caring for patients with CF, there is a lack of consensus on which items are most helpful in diagnosing pulmonary exacerbations requiring treatment. In addition, there is a difference in which items are helpful between pediatric and adult patients. Some signs and symptoms have been shown to be strongly associated with pulmonary exacerbation requiring therapy.

How to recognize symptoms and signs? Respiratory symptoms include increased cough, increased sputum (phlegm) production, chest congestion, and decreased exercise tolerance. General symptoms include increased fatigue, absence from school or work, decreased appetite, and weight loss. Other symptoms could include changes in sputum appearance (color, bloody), fever, or shortness of breath. Signs include increased work of breathing, increased abnormal breath sounds on lung examination, and weight loss of ≥1kg over the past month. Diagnostic tests include lung function test (spirometry) and chest radiography (chest x-ray). Pulmonary exacerbation can cause a significant change in measurements of lung obstruction. Chest x-rays may show abnormalities during pulmonary exacerbation but can also be unchanged from a patient’s prior images.

When to contact your CF center? With the onset or persistence of any of the symptoms listed above, patients and/or caregivers should contact their CF nurse coordinator or CF physician on-call to discuss the details of those symptoms. The provider and patient (or caregiver) will decide on the need for follow up, further evaluation, and/or treatment. If there are questions about symptoms or signs, it is best to err on the side of contacting your CF center and clarify your questions.

What causes pulmonary exacerbations? A variety of things can cause or precipitate a pulmonary exacerbation.
ing or inconsistent use of maintenance CF therapy can lead to a pulmonary exacerbation. Lack of time, non-functional equipment, or lack of medications can lead to suboptimal adherence to prescribed CF therapies. Viral infections such as common cold viruses, respiratory syncytial virus (November to April), and the influenza virus, (October to March) can cause pulmonary exacerbations in patients with CF. In patients with CF, viral infections in combination with ongoing airway inflammation and lung obstruction can cause more severe illness than in patients without CF.

Mucus plugging from chronic inflammation, mucus production, and chronic bacterial infection can lead to a collapse or blockage of portions of the lung. This can lead to increased respiratory symptoms. Collapsed portions of the lungs need to be treated aggressively because without treatment, it can lead to the development of bronchiectasis (damage and distortion of the airways).

Patients with fungal sensitivity (allergic bronchopulmonary aspergillosis) can also have symptoms of pulmonary exacerbation during flares of the allergic disease. These flares also require evaluation and treatment.

Chronic infection with atypical mycobacteria can also cause symptoms of pulmonary exacerbation during flares of the allergic disease. These flares also require evaluation and treatment. Atypical mycobacteria are found in the environment such as in soil, streams, and rivers. Atypical mycobacteria are estimated to affect about 13% of patients with CF in the United States. The two most common mycobacterium species in patients with CF are Mycobacterium avium complex and Mycobacterium abscessus.

Why do pulmonary exacerbations need to be treated? Pulmonary exacerbations cause significant pulmonary and general symptoms that can be disruptive to school and work and diminish a patient’s overall quality of life. Pulmonary exacerbations should be recognized early and treated swiftly to relieve a patient’s symptoms. Decline in lung function and shorter life span are also associated with pulmonary exacerbations; therefore, these episodes should be treated aggressively to help preserve lung function.

How are pulmonary exacerbations treated? Patients with symptoms of pulmonary exacerbation are evaluated with physical examination, lung function testing (spirometry), chest imaging, and sputum culture and laboratory testing as needed. Depending on the severity of the pulmonary exacerbation, patients may be treated at home or hospitalized. Usually patients are hospitalized then transitioned to further care at home when appropriate. The main components of treatment include chest physiotherapy, mucolytics, antibiotics, and optimal hydration and nutritional intake. Chest physiotherapy (high frequency chest wall oscillation, oscillatory positive expiratory pressure, manual percussion and postural drainage) are increased in frequency, up to 4-5 times a day. This is to help move secretions and mucus up and out of the lungs. Mucolytics (sodium chloride, dornase alpha, acetylcysteine) are paired with chest physiotherapy to break up and facilitate mobilization of mucus. Bronchodilators (albuterol) are used to relieve obstruction and help mobilize of mucus. Antibiotics are used to treat chronic and new pulmonary bacterial infections. Antibiotics are usually delivered directly to the blood stream (intravenously). For some circumstances, milder pulmonary exacerbations are treated with oral antibiotics if an oral form of the appropriate antibiotic is available.

A patient’s nutritional status is very important to lung health and recovery from pulmonary exacerbation. During pulmonary exacerbation, a patient’s appetite may be very low and the intake of food and supplemental nutrition by mouth could be insufficient. In this situation, patients may need supplemental nutrition by tube feeding directly into the stomach.

Treatment of pulmonary exacerbations is labor intensive and time consuming. Because of this, many patients are hospitalized for their therapy during these episodes. Intense treatment can last from 10-14 days or more if necessary.

How to prevent pulmonary exacerbations? Keeping up with prescribed airway clearance therapies, medications, and nutrition in patients with CF is crucial to maintaining good lung health.

Good hand hygiene is necessary to limit the spread of germs, including viruses and bacteria. Routine cleaning of your respiratory equipment can also help stop the spread of germs. Annual immunizations to influenza can be helpful to improve your immune response to the virus if you are exposed from other sick individuals.
**Additional Reading:**

CF Foundation Respiratory Care Guidelines [link to guidelines]

CF Foundation Staying Healthy [link to staying healthy]

**References:**

5. Sanders DB, Bittner RC, Rosenfeld M, Redding GJ, Gas CH. Pulmonary exacerbations are associated with subsequent FEV1 decline in both adults and children with cystic fibrosis. Pediatr Pulmonol. Apr 2011;46(4):393-400.

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**The FLU**

BY CARLOS MILLA, MD

Many viruses that produce respiratory infections which can cause pulmonary exacerbations circulate throughout the year. However during the fall and winter months, certain viruses become more widespread and predominate as reason for illness in the community. One of these is the Influenza virus, known as the ‘flu’ for short. Epidemics of the flu occur every year, though from year to year there is some variability on the timing of its onset, severity and duration. An important fact to keep in mind about the flu is that the virus changes almost constantly, so it is not surprising to see new strains appearing periodically. At the time of this writing the flu season has already reached epidemic levels in many parts of the country, including California. The virus type that is circulating the most heavily is the strain known as Influenza H1N1. This strain is contained in the influenza vaccine (‘flu shot’) that became available last fall (as well as the H3N2 virus and the flu B virus). The current recommendation is for anyone older than age 6 months to be immunized, and particularly people with chronic respiratory conditions such as CF. At the Stanford CF center we take this quite seriously and according to our most recent statistics 99.6% of our patients have been immunized. If you have not received a flu shot yet, please do so as soon as possible since there is no downside in getting it late. You must also take into account that you could still become sick with the flu despite being immunized. Fortunately, from the information available so far this does not seem to be occurring too often. Antiviral medications are available and could be effective against the currently circulating strains if started shortly after the onset of illness. It is also important to take additional precautions including staying away from sick people and washing (or sanitizing) your hands frequently to reduce the spread of germs. If you do fall sick with the flu, please contact your nurse coordinator immediately for advice and stay home from work or school to prevent spreading influenza to others.

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**New Pediatric Staff Members**

**Sruthu Veeravalli**

Sruthu Veeravalli graduated with her Bachelor’s degree from University of Texas at Dallas in Information Systems and went on to complete her Master of Social Work at the University of Southern California in May 2012. Sruthi came to Lucile-Packard Children’s Hospital in August 2012 as a Social Work Fellow working in the Intensive Care Units. Sruthi recently accepted the position as the Pediatric Cystic Fibrosis and Outpatient Pulmonary Social Worker this month. Originally from Texas, Sruthi is a southern lady at heart who loves cooking/baking, dancing, and hiking.
Chia seeds have gained popularity and attention over the past year because of its nutritional properties that make it a functional food similar to flaxseed. The seeds are from the Salvia hispanica plant, the seeds that grow into sprouts for the infamous Chia Pets. Chia seeds originated in South and Central America where it grows well in the arid environment. At present there is limited research to support its efficacy for management of cardiovascular disease risk factors.

The seeds can now be found in most supermarkets and health stores where its nutritional composition makes it comparable to ground flaxseed as a rich source of omega-3 fatty acids, iron, and calcium. The seeds are small and round in appearance and can be digested in the intestinal tract without needing to be ground first as with flaxseed. The small seeds pack quite a nutritional punch per one ounce serving (approximately two tablespoons): around 3,000 micrograms of omega-3 fatty acids, 5 grams protein, a good source of calcium, and 5 grams of soluble fiber. Patients currently on warfarin (Coumadin) therapy should not consume chia seeds due to concern for nutrient-medication interactions.

Chia seeds are marketed as a functional food due to their possible benefits for cardiovascular disease management. The omega-3: omega-6 composition of the seeds is 3:1, which is within the desirable range for cholesterol management. As a result of this fat ratio, chia seeds have been reported to help lower blood pressure, decrease LDL (“undesirable”) cholesterol levels, decrease total cholesterol levels, and decrease serum triglyceride levels. Consistent consumption is reported to also help increase HDL (“desirable”) cholesterol level.

Chia seeds do not have a strong taste and can be added to a variety of foods and drinks. The small seeds are water soluble and are very efficient at absorbing water, creating a gelatinous consistency. The seeds may be consumed raw, sprouted, ground, cooked, or made into a gel. The seeds can be sprinkled as a topper for yogurts, hot cereals, potatoes, and grain-based dishes. Chia seed flour, gluten-free flour, is available commercially and can be used as a one to one substitution for other flours. Chia seed flour should be sifted prior to using in the recipe and it may increase the baking time by a few minutes.

Chia seeds are generally recognized as safe as a functional food and supplement by the Food and Drug Administration. The nutritional composition of the seeds may make them a comparable supplement to ground flaxseeds for management of cardiovascular disease risk factors. Currently, there is little evidenced-based research to support the functional claims for daily consumption of the seeds so there is no guarantee that the reported benefits can be achieved. However, chia seeds are a nutrient dense food and may serve as a healthy addition to one’s diet.

**California Chicken**  (serves 4)

<table>
<thead>
<tr>
<th>8 boneless chicken breasts</th>
<th>1/2 cup white wine</th>
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<tbody>
<tr>
<td>2 cups sour cream</td>
<td>2 cups cheddar cheese, grated</td>
</tr>
<tr>
<td>1 can cream of mushroom soup</td>
<td>1 can french fried onion rings</td>
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Place chicken breasts in greased 13 x 9 baking dish. Mix together sour cream, soup and wine, pour over chicken. Top with cheese and onion rings. Bake at 325 degrees for one hour. Serve over rice or noodles.
While the annual European CF Society Conferences have been rapidly growing in attendance and importance, the annual NACFC remains the world’s largest and most important place for CF researchers and health professionals of all disciplines to meet, present new information, and network. The most recent NACFC, held October 2013 in Salt Lake City, with its thousands of registrants and nearly 700 individual study presentations, was, in my view, most notably memorable for projects that translated breakthrough discoveries in new gene-based “personalized medicine” treatments for CF into fresh and comprehensive insights as to how fundamental therapies affect people with CF.

Such a focus can tell us how “fixing” the CF gene or protein actually works at the tissue, organ and whole person levels. An outstanding example of this approach is the GOAL (G551D Observational) study, an ongoing CFF funded multicenter project aimed at finding out how an effective fundamental CF drug, ivacaftor, actually works and affects people with CF and gene mutation for whom it was found startlingly effective and approved with record speed by the FDA in early 2012. In this study people receiving ivacaftor on-label (a G551D mutation and age 6 or higher) and post-marketing approval have been followed for continuing assessments of response and current status. Most patients were further enrolled into smaller focused GOAL “substudies” thoughtfully broken down into state-of-the-art approaches to better understand how really effective therapy works in different organs, providing a template for much future clinical research in CF. The first wave of results from the GOAL study were presented at NACFC at a number of sessions.

What can this teach us? One example is the tremendous improvement in nutritional status, usually most noticed by big weight gains, in folks taking ivacaftor – why is that? A substudy using an ingenious “smart pill” sensor passing through the GI tract found that ivacaftor decreases intestinal acidity in such a way as to enhance absorption of nutrients, a likely mechanism for the nutritional benefit observed. Another substudy found that ivacaftor increases directly measured lung mucus clearance two-fold in the larger airways and five-fold in the smaller airways, a likely mechanism for the big improvements in lung function observed. A third exciting albeit preliminary finding was an unexpected drop in positive Pseudomonas sputum cultures from about 55% to 35%, suggesting that longer-term a fundamental treatment may actually contribute to the lung healing itself by finally starting to get rid of persistent infection. Perhaps most important, the GOAL study has verified pivotal clinical trial efficacy results with real-world effectiveness by substantiating that the striking improvements in lung function, hospitalization and intravenous antibiotic use, weight and body mass index, and quality of life measures seen in the clinical trials are also seen, and to a similar degree, in routine clinical care, and with a similar highly satisfactory safety profile.

The GOAL study shows how research in CF, while beginning in the basic science lab, and moving through a painstaking and expensive biopharmaceutical company-academic partnership of development, clinical trials, and regulatory processes to approval and marketing, continues in routine clinical care and practice through the CF Center network, the national Registry and other databases, further sponsored research grants addressing new hypotheses, and real world effectiveness projects.

The CF model of how to care for difficult and serious chronic disease continues to blaze the pathway to how personalized medicine will work in the 21st century, and provides hope to CF patients and families anxiously awaiting the next wave of effective fundamental therapies (coming soon to clinic near you!): the 95% of patients not so fortunate as to have something like ivacaftor in their medicine cabinet – yet. Finally, projects like the GOAL study re-emphasize the absolutely critical role of patient and family participation in clinical trials, whether of investigational or approved drugs, to keep raising the bar on CF to the final goal, a healthy and long life.
Cystic Fibrosis Parent Advisory Council Update: Supporting Patients and Families with CFRD

BY SIRI VAETH, MSW

The CF Parent Advisory Council works in partnership with members of the CF Care Team to improve communication between families and the team, address unmet needs, and improve quality of service delivery. Recently, the Council has been actively discussing the issue of cystic fibrosis related diabetes (CFRD), and potential ways to support patients and their families who are seen by the endocrinology clinic. As most families know, the CF Center at LPCH begins testing children for cystic fibrosis related diabetes at age six. Research consistently documents that poorly controlled CFRD is directly linked to decreased lung function and survival, and the center seeks to educate all families about the importance of diagnosis and management, while acknowledging the increased physical and emotional burden of this diagnosis. For parents and young people who are juggling the many responsibilities related to their CF care, the additional responsibility of blood sugar testing and insulin injections may seem overwhelming. For some families, the difference in the CF and endocrinology clinics’ care models adds to the challenge.

Members of the CF Parent Advisory Council are working to identify areas in which improvements can be made to better support patients with CFRD. If you have suggestions, or want to share your experience, we want to hear from you. Either go to the CF Center website (http://cfcenter.stanford.edu), where there is a link on the homepage to leave anonymous feedback, or email Siri Vaeth, Council Lead Parent, at svaeth@lpch.org. The input of Center families is encouraged.

Why I Participate in Research Studies

BY JULIE PHILLIPS, CF PATIENT AND RESEARCH SUBJECT

Having the opportunity to participate in research studies has been such a blessing. Throughout my seventeen years of life, I’ve been in many studies. Whether it’s just filling out a quick survey, giving blood work or a sputum culture, or having to do months of testing out a new medicine, whenever I am asked to be in a study, my answer is always yes. The only way new drugs can get FDA approved and get out onto the market is for it to go through the clinical trials process. Clinical trials can’t happen and new medicines that can potentially improve the health of cystic fibrosis patients can’t be made available without “people participation”. That’s why I say yes to every study I am eligible and asked to be a part of. Living with a life threatening disease is hard work. I can go from 100% lung function one week to 80% the next. I am compliant with my daily treatments but that doesn’t guarantee that a new bacteria won’t enter my lungs. When I’m asked to test out a new drug, I feel like a kid on Christmas. Even though I don’t know if I am getting placebo or the real deal, it’s still just as exciting knowing that I could be receiving a medicine that could possibly change my life. If given the opportunity to change someone’s life forever, wouldn’t you do it? Participating in research studies is the best decision I have ever made and I hope that maybe just one person will read this and change their mind about being a part of changing and improving lives.
ACFAC has created a wallet-sized resource card for newly-diagnosed CFRD patients. Ask Lara, Kathy or Meg for a card at your next clinic visit. And if you’re having trouble getting to clinic, ask Meg about gas cards, hotel vouchers, and transit information, provided by funds raised by ACFAC members.

And we all know we must take care of ourselves at this time of year, with increased stress and changing weather. CF mentors are here to help you! Co-sponsored by ACFAC along with the heart transplant and other advisory councils, the Stanford Peer2Peer program matches mentors and patients for phone support; talk to your CF social worker if you’d like to be assigned a mentor or if you’d like to train to become one.

Elika Rad, Advanced Practice Nurse Practitioner, will provide clinical leadership for Cystic Fibrosis care for inpatient protocols. Ms Rad has distinguished herself as a caring and sensitive provider for our adult patients. In conjunction with Dr Paul Mohabir, Ms Rad will develop Clinical Strategies that will guide the daily operations of our adult program and provide support to our entire CF team. Process Excellence at Stanford is working with the Pulmonary Critical Care faculty to bring more clinical services to the clinic space so that outpatients can experience a more efficient clinic visit.

The sick call process for adult cystic fibrosis patients requires a direct phone discussion with patient and provider to assess symptoms and to triage for clinical emergencies. All sick calls are discussed with a nurse practitioner and are reported to the Attending Pulmonologist.

All adult cystic fibrosis patients referred to Stanford Emergency Department for assessment by the Pulmonary Fellow, Nurse Practitioner or Coordinator are reported to the Callback RN in the Emergency Department. Upon completion of the initial assessment by the Emergency Department, your Adult Cystic Fibrosis team is contacted. Please call your adult cystic fibrosis team so that we can improve your experience at Stanford.

Meg Dvorak, MSW, is working to offer an advanced directive alternative, “Five Wishes” to our adult cystic fibrosis patients. “Five Wishes” allows greater leeway for you as a patient to express your wishes to those who most care for you.

Annual review for adult cystic fibrosis patients will be consolidated in 2014 into a single testing period between February 1st to May 1st. Each patient will receive a letter outlining the necessary tests and contact numbers to schedule certain procedures. Upon completion of all tests, your results will be reviewed with you in your clinic visit.
Pediatric CF Center Update

BY MARY HELMERS, RN

At the end of December, we completed our teaching topics for the Quality Improvement Project (aka: the CF Binder project), which addresses the educational needs of our patients and families. Thank you again to all our families and patients who have assisted in our data collection for the project. Starting in January 2014, we will be re-administering the educational assessment. We are excited to see everyone’s progress!

Our new clinic space at 770 has been open since August 3rd and we hope you are all happy with the new clinic. If you have any suggestions, concerns, or comments regarding the new clinic, please feel free to give us your feedback when you are in clinic or via email: mhelmers@lpch.org (Mary Helmers, RN, CF Nurse Coordinator) or ebeken@lpch.org (Liz Beken, RN, CF Clinic Nurse).

Reminder!! Wear your mask. We have new turquoise colored masks (N95) that we are asking all CF patients to wear. They are being handed out at the front desk. These masks have smaller filters which allow for more protection when walking outside during the construction. We would like all patients to wear them to and from all clinics/hospital, and when you walk outside the medical center. They should fit snugly around the nose and mouth. If you have not received the new mask, ask the front desk staff or anyone from the CF Team.