

# Cystic Fibrosis Center News

## Introduction to CFTR Modulators

– Denise Kwong, Pharm.D., BCPS

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are small-molecule drugs that interact with the defective CFTR channel to help it function. The first CFTR modulator, ivacaftor (Kalydeco), was approved by the FDA in 2012, and since then, two more combination therapies have become available in the United States. The combination therapies are lumacaftor/ivacaftor (Orkambi) and tezacaftor/ivacaftor (Symdeko).

CFTR modulators are further subcategorized as potentiators and correctors. Ivacaftor is a CFTR potentiator that helps keep the CFTR channel open at the cell surface to increase chloride transport.

Lumacaftor and tezacaftor are both CFTR correctors that help the defective CFTR protein fold correctly so that it can reach the cell surface.

### How to take CFTR modulators:

- Improve absorption by taking with food that contains fat. Examples include cheese pizza, eggs, butter, peanut butter and whole-milk dairy products.
- Ivacaftor and lumacaftor/ivacaftor come in granule packets in addition to tablets. Empty entire packet; mix in 1 teaspoon (5 ml) of soft food or liquid that is room temperature or colder. Take within one hour.

### *In this issue*

Introduction to CFTR Modulators .....	1	Cystic Fibrosis Parent Advisory Council .....	13
Inhaled Antibiotics .....	3	Tips to Support Your Child's Physical Activity and Exercise as He or She Gets Older .....	14
My Journey to a Double Lung Transplant.....	4	Why Transition Matters .....	15
Pediatric CF Center Update.....	6	CF Word Search .....	16
Stanford Adult Cystic Fibrosis Advisory Council.....	7	Current Research Studies .....	17
Healthy High-Calorie Options for Cystic Fibrosis Patients .....	8	Cystic Fibrosis Center at Stanford.....	19
20th Annual CF Education Day March 15, 2019 .....	9	New Pediatric Clinic Staff Member .....	20

- Timing is important. Doses are usually spaced 12 hours apart so that drug levels stay consistent throughout the day. Take a missed dose with a fat-containing snack as soon as you remember, but if it's been more than six hours, skip the missed dose. Tezacaftor/ivacaftor tablets are color-coded, and morning and evening doses are designated, because the components are different. The blue tablet only has ivacaftor, whereas the yellow tablets and white tablets are formulated with both tezacaftor and ivacaftor. *See image below*
- It may take up to two weeks before you see the effects of CFTR modulators on chloride channels.



Symdeko is a cystic fibrosis transmembrane conductance regulator (CFTR) modulator.

**Drugs and food interactions:**

- Dose adjustments for liver function and drug interactions are necessary to avoid toxicity. Liver metabolism changes medications into a format that the body can eliminate. Ask your health care provider before starting new medications, herbal supplements or vitamins to screen for interactions.
- Certain medications and herbal supplements are not recommended, as they decrease the effectiveness and enhance the liver's ability to process and eliminate CFTR

modulators. Some examples include rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin and St. John's wort.

- Avoid foods like Seville oranges and grapefruit, because they change the liver's ability to eliminate CFTR modulators and can lead to toxicity.
- The lumacaftor component in Orkambi decreases the concentration of other medications and may make them less effective. Among these are hormonal contraceptives, so alternative forms of contraception are recommended instead.

**Warnings/possible side effects:**

- Dizziness is a common side effect, so avoid driving or other activities that require a lot of coordination when starting this medication to see how your body reacts first.
- Other common side effects include headache, nausea and sinus congestion.
- Other less common but more serious side effects include allergic reactions (itching, hives, throat swelling, trouble breathing), cataracts (blurred vision) and liver toxicity (dark urine, pale stools, stomach pain, yellowing of skin and eyes). Call your health care provider right away to report these symptoms.
- Lumacaftor/ivacaftor has additional side effects, including shortness of breath, chest tightness, high blood pressure, and irregular or missed menses.

**How to monitor CFTR modulators:**

Regular CF clinic visits are important in order to monitor how you are doing on your therapies. In addition to assessing lung function, you may have additional blood work done to monitor your liver function. An annual eye exam is recommended to monitor for cataracts.

- Switching between CFTR modulators may require additional monitoring and dose adjustments to other medications since the drug-interaction and side-effect profile is slightly different for each CFTR modulator.

### Other considerations

Make sure to bring your CFTR modulator when being admitted to the hospital because this is a specialty medication and will not be readily available at every hospital.

## Inhaled Antibiotics

– *Russell Wise, Pharm.D.*

Infections in the lung are a primary cause of illness for people with cystic fibrosis. The reduced hydration of the lungs caused by dysfunctional CFTR channels leads to thick, sticky mucus that builds up in the airways. This creates the optimal living environment for certain bacterial organisms commonly encountered in everyday life.

When an organism repeatedly shows up in cultures despite antibiotic treatment, this is typically referred to as colonization. The most common bacteria colonized in the lungs of people with cystic fibrosis are *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Bacterial colonization in the lung can cause inflammation, which often leads to the symptoms of sickness that many patients feel, including fever, cough and increased mucus production.

Antibiotics have long been a backbone in treatment regimens for cystic fibrosis. Advances in the development of new antibiotics and delivery methods over the years have played a large role in the steadily climbing life expectancy for people living with cystic fibrosis. Physicians have long sought to deliver antibiotics directly to the lungs, ground zero for these chronic infections. The benefit of antibiotic delivery via inhalation is the ability to deliver therapeutic dosages directly to the primary site of infection while

minimizing the risks of systemic toxicity and side effects. However, sometimes the mucus is just too thick for inhaled antibiotics to be fully effective at the site of action, so intravenous antibiotics are used to treat the infection.

Among the most common inhaled antibiotics for *Staphylococcus* and *Pseudomonas* in cystic fibrosis are tobramycin, Cayston, and colistin. Local and national bacterial resistance patterns help the medical team better determine which inhaled antibiotic will be best for each individual patient.

Originally, the intravenous formulations of these antibiotics were nebulized to deliver medication locally to the lungs. In recent years, drug companies have developed formulations that have characteristics specifically designed to enhance their use via the inhaled route and are now staples in treatment of the cystic fibrosis lung infection.

### Specialized inhaled antibiotic formulations:

**Tobramycin:** TOBI® Podhaler™, TOBI®, Bethkis®, Kitabis®

**Aztreonam:** Cayston®

**Amikacin:** Arikayce®

### In clinical trials:

**Vancomycin:** AeroVanc™

**Levofloxacin:** Quinsair™

# My Journey to a Double Lung Transplant

— Elyse Elconin-Goldberg (six years post double lung transplant)

It seems very fitting that I should be writing this article on my transplant journey as my son graduated from college this past June, an event that I am so grateful to have experienced. I had a double lung transplant on September 17, 2013.

I was diagnosed with CF when I was 3 years old, and I turned 60 this past January. My husband and I created a family through adoption. My daughter is 26 and my son is 22. We also now have a new grandson! Who would have thought I would live long enough with CF to become a grandmother! I have always said that having CF was like having a third child. At many times over the years, my CF required as much, if not more, attention than my family.

I truly believe having a family gave me the internal motivation to work as hard as I could to stay on top of my CF. It takes a strong partnership in your marriage to manage the CF roller coaster. Along with being incredibly compliant with all of my breathing treatments, I have always been an avid exercise enthusiast. In November 2012, I caught the Respiratory Syncytial Virus (RSV). This was a game changer for me and ultimately led me down the path necessitating a double lung transplant.

Post RSV, my lung function FEV1 hovered around 28 percent. My world got much smaller, and doing ordinary tasks became more and more difficult. I was getting more frequent infections that required much longer hospitalizations. My children were in their late teens at this point, but I could see the toll this was taking on their lives. By January 2013, I was on oxygen full-time. I still pushed myself to exercise daily, but it was excruciatingly exhausting and challenging.



Elyse, center left, with her family.

During a hospitalization in March 2013, a former doctor of mine came to visit me. She was the first to bring up the idea that I needed to start considering transplant. She told me a critical factor in transplant is that you need to be sick enough to need a transplant but well enough to survive it. At my next clinic visit, the CF team brought up the subject of transplant. The emotions I went through realizing I had reached end-stage CF were daunting. I thank my medical team for not waiting any longer to bring up the idea of transplant.

Very soon after deciding to consider transplant, I was hospitalized again for a CF exacerbation. I asked if the required testing for the evaluation process could begin while I was an inpatient. Gratefully, I passed all of the tests and was accepted into the Stanford double lung transplant program. Then the waiting began. In my mind, I had so many emotions, ranging from fear of the surgery and postsurgery pain to the challenges that recovery might present.

I am a fairly optimistic person, so I tried to stay away from the negative what-ifs that I could not control and focus on what I could control. Once again, exercise was a key survival component. I literally trained for my transplant! This proved to be incredibly beneficial in my posttransplant recovery.

I was on the transplant list for two months as my health rapidly declined. When I got “the call,” I was playing mah-jongg with friends. It was a blur of activity getting home to pick up the items that I had planned to take with me, to call family, and to get to Stanford. My surgery lasted seven hours. That first breath after being extubated was unbelievably amazing! Almost immediately, I was off of any oxygen. Those first few days postsurgery were uncomfortable. Pain management was a top priority, but I’ll admit that it hurt! I was discharged 10 days after my surgery. What an amazing feeling coming home to find that all of the medical equipment I needed to breathe had been removed from our home.

With transplant, the necessary medications are almost entirely different from those taken in your pretransplant life. The number of medications and their schedules take some time to get used to. The first three months posttransplant, a patient has to have 24/7 care by a family member or friend. This is in part due to the enormity of the surgery, but also the postsurgical pain medications and transplant medications can cause some brain fog.

Immediately after settling into being home, I was aware that my life had taken a 180-degree turn for the better. Not having to spend six to eight hours a day doing breathing treatments, I gained so much time in my day. As my pain diminished, I began pulmonary rehabilitation.

The biggest challenge I am facing posttransplant is skin cancer, which is a result of immunotherapy medications. I have had several surgeries and now always wear sunscreen, a protective hat and SPF clothing. As I have become an avid hiker, I try to find shadier trails and stay out of the sun between 11 a.m. and 4 p.m.

Today my life is so full with family, friends, travel, volunteering and, of course, exercising. To celebrate my gratitude for my donor and donor’s family, seven months posttransplant, my two friends on my care team and I walked a half marathon!

Transplant life has far exceeded my greatest expectations. When I reflect on what this gift of life has given me, I cherish the time with family, friends and one of the little things, spontaneity. I wish to express my eternal gratitude to my donor and donor’s family for this Gift of Life.

Lastly, a big thank-you to the Lung Transplant team and the Adult Cystic Fibrosis Team at Stanford. This journey takes a village, and I am so incredibly appreciative for those that I have met along the way through a double lung transplant.

# Pediatric CF Center Update

– Mary Helmers, RN

## Don't forget! Get your flu vaccine!

Check out the [Cystic Fibrosis Center at Stanford](#) website.

## The following information is on our center's website:

**Help with PG&E bill:** Did you know that you can get assistance with your PG&E bill? PG&E forms for medical equipment/devices can be found on the PG&E website under Medical Baseline Allowance Application for Medical Baseline Enrollment and Recertification. All you need to do is print the form; fill it out, listing all your medical devices (e.g., nebulizer/compressor; if you use oxygen, CPAP or BIPAP); and bring the form with you to your next CF clinic visit. Your provider will sign it; then you mail the form to PG&E.

**CF Clinic Prep form (patient update):** This form was designed to help you get all your questions answered. This is not mandatory, but a tool to assist you in jogging your memory in preparation for your clinic visit. Do you drive away from clinic thinking, "Oh no, I forgot to ask such-and-such question"? You can now fill out this form ahead of time and bring it to your clinic appointment.

## Helpful reminders

**MyChart (secure electronic correspondence):** If you have not signed up already, please sign up for MyChart at your next clinic visit. MyChart is a secure way to communicate with your provider and CF care team. The CF care team cannot respond to regular patient/parent emails, since they are not secure so please note that any emails sent to the team will be responded to with a phone call. We do not always check emails on a daily basis, so if you or your child has a clinical need or question, please call the CF RN line at (650) 736-1359.

It takes only a minute to sign up—one of the front desk staff will be happy to assist you.

*To help expedite your clinic visit, please remember to bring your CF binder and the most recent CF action plan with you to clinic.*

## Prescriptions

Just a reminder that your prescription request can take up to 72 hours to be processed. This has always been our policy; however, we strive to turn them around sooner. Please keep in mind that even after we send the prescription to the pharmacy, it can still take another 48 to 72 hours for the pharmacy to process (especially mail order pharmacies). It is important for you to stay on top of your refills and request them at least one week before you are due to run out.

## Helpful hints for requesting refills:

- Call your pharmacy first to find out if you have refills.
- If you have a refill, great! Then they will process.
- Your pharmacy should call us if you have no refills.

**Remember:** We cannot guarantee that your request will be filled the same day or within 24 hours.

## CF Passport

**Parents:** Please remember to carry your child's CF Passport in your wallet. The CF Clinic sent the Passports out in the mail to each family; however, it has been over a year. If for some reason you did not see, tossed, or may not have received the Passport, please ask for one when you come to your next clinic appointment. We now have them in English and Spanish.

## Annuals

Remember, our goal is to get all annual testing done on or around your child's birthday. At your clinic visit three months prior to when your annuals are due, the CF RN will review with you what is due. Please feel free to ask us, too.

## Wear your mask

We have turquoise-colored masks that we ask all pediatric 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. 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.

Patients can also wear a Vogmask (a microfiber, high-filter mask with vents).

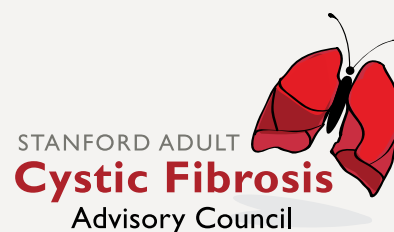


Vogmask

### CYSTIC FIBROSIS PASSPORT

- Please escort me to a private room
- Please follow contact/droplet precautions (see CF Isolation Policy)
- Gown, mask, gloves for all health care providers
- Clean all surfaces after patient contact
- Please remember to use good hand washing/gel/foam cleanser before and after patient contact

CF Passport sample



# Stanford Adult Cystic Fibrosis Advisory Council

— *Brian Eddy*

The council continues to work on multiple projects to benefit the CF community at Stanford. The most important project is to have a piece of artwork in the new Stanford Hospital dedicated to those patients we have lost to CF. Thanks to a generous and caring benefactor, the space has been reserved and the artwork has been selected by the council members. We are now working on the wording that will go on the plaque accompanying the artwork.

In addition, several other projects have been completed. First is a pamphlet describing the transplant process from the point of view of a CF patient, which provides a significant amount of useful information. Second is a pamphlet providing information on masks and their usage. For more information about the council, please visit our [website](#).

# Healthy High-Calorie Options for Cystic Fibrosis Patients

– Julie Matel, RD

Consuming a high-calorie diet is recommended for individuals with cystic fibrosis in order to achieve optimal growth in children, promote a healthy weight in adults, and prevent a decline in lung function. As people with CF are living longer, it is also important to consider a wide variety of healthy foods as part of an overall balanced diet, with emphasis on nutrient density. Here are some ideas for high-calorie, nutrient-dense foods to incorporate in meals and snacks.

## Breakfast ideas:

- Oatmeal or whole-grain waffles with added butter / nut butter / tsp. of olive or canola oil, maple syrup, banana, nuts, dark chocolate, and/or dried fruits (raisins, cranberries)
- Scrambled eggs or omelet made with whole milk / added avocado, veggies and shredded cheese
- Cinnamon raisin English muffin or bagels topped with nut butter and banana
- Fruit muffins (pumpkin, blueberry, apple); warm and drizzle with butter

## Lunch ideas:

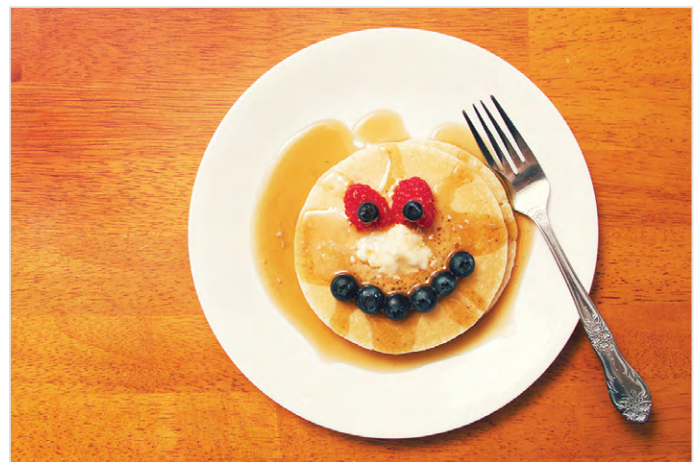
- Mac and cheese with added cauliflower
- Add oil/cream to tomato soup
- Turkey or chicken on whole-grain bread topped with pesto sauce, cheese and/ or avocado, spinach and tomatoes
- Cheese tortellini mixed with pesto
- Tuna or egg salad sandwich mixed with olive oil-based mayonnaise

## Dinner ideas:

- Salmon with olive or avocado oil
- Sweet potato mashed with butter; roasted potatoes made with olive oil
- Salad with toppings (cranberries, nuts, shredded cheese, dressing)
- Homemade pizza (whole-grain dough with pesto or tomato sauce, olives, pepperoni, cheese)
- Hamburger topped with avocado and cheese, serve with sweet potato fries

## Snack ideas:

- Fill pita bread with hummus and vegetables
- Peanut butter-filled pretzels
- Trail mix
- Smoothies
- Crackers and cheese
- Yogurt parfait topped with granola



*Continues on page 18*



# 20th Annual CF Education Day

## March 15, 2019

– *Monica Elazar, Regulatory Affairs Specialist*

### Morning session

Dr. Carlos Milla, Pulmonary Division CF Center director, pediatrics, welcomed the audience and introduced the first speaker. **Dr. Michael Boyle** from the CF Foundation, launched into his presentation, “What Is New and Exciting in CF Research.” Dr. Boyle began with a refresher on cystic fibrosis transmembrane conductance regulator (CFTR) and continued with an update on where we are today with modulator therapy.

He discussed the expansion of Kalydeco use to children ages 1 to 2 years and Orkambi to children ages 2 to 5 years, and FDA approval of Symdeko. He reviewed the results of triple combination Phase 2 trials of VX-659 (with TEZ/IVA) and VX-445 (with TEZ/IVA) and the current expected timeline of the approval of triple combination therapy and what that approval will mean. Dr. Boyle gave updates of the Therapeutics Development Network (TDN) PROMISE Study and listed some of the CFF’s funded research activity:

- \$72 million committed to date to Nonsense and Rare Mutations Research and Therapeutics Initiative.
- More than 50 percent of CFFT Lab research is focused on nonsense mutations.
- Up to \$11 million awarded in 2018 to a biotech company to screen more than 2 million compounds.

Dr. Boyle continued on with a brief overview of the many labs participating in CFTR theratyping, nonsense and RNA programs. He discussed in detail continued progress of gene therapy and gene editing and again reiterated the pledges of leaving no one behind and CFTR treatment for all.

When it comes to treating complications, Dr. Boyle noted that the CFF is currently engaged with 172 companies—an addition of 69 new companies in 2018! CFF is in talks with an additional 17 companies for potential therapeutics and is committing \$100 million over the next five years to infection research to improve detection, diagnosis, treatment and outcomes of infections in people with CF. Finally, Dr. Boyle reviewed survey results listing the CF community priorities, showed a map of all CFF TDN and global trial networks, and described an exciting year to come as part of CFF long-term planning.

**Dr. Paul Mohabir**, director, Adult Cystic Fibrosis program, presented “The State of the Stanford CF Center” updates. Dr. Mohabir began by reminding us of the center’s mission 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. He reviewed some highlights from the Cystic Fibrosis Foundation 2017 Patient Registry Annual Data Report and the Stanford CF Center Report. He spoke about the rising education level and socioeconomic status of CF patients, the rising number of pregnancies in women ages 14 to 45 in the 10-year span ending 2017, the change in proportion of prevalence of respiratory microorganisms from 1991 to August 2017, bacteria culture data seen in 2017, CF modulator therapies—the timeline of ivacaftor eligibility change from 2012 to 2017, complications, and the survival median age predicted from 1986 to 2017 (now 46.2 years).

Dr. Mohabir reviewed ongoing commitments of the Stanford CF Center to clinical quality improvement, program growth, education and implementation, access to care, compliance and screening, multidisciplinary care and outcomes.

The Cystic Fibrosis Center at Stanford is one of only a few centers in the United States with an active lung transplant program and the only CF center in California with Translational Therapeutics Development Center designation, and Lucile Packard Children's Hospital Stanford has the only pediatric lung transplant program west of the Rockies.

**Dr. Carlos Milla** then discussed the pediatric program and how the mission described by Dr. Mohabir is accomplished “through highly dedicated and focused collaborative transdisciplinary work and in close partnership with our patients and families.” He described the center's organizational structure, Stanford's network of locations and physicians, and the challenges of covering a referral area of more than 700 patients. He spoke about what defines “translational medicine to its full potential.”

At the Cystic Fibrosis Center at Stanford, the goal is for every patient to have the following:

- CFTR genetics fully identified
- CFTR functional status fully characterized
- CFTR theratype (drug responsiveness) characterized
- Mental health assessed at least yearly
- Quality of life assessed longitudinally
- Treatment-adherence parameters monitored longitudinally
- Satisfaction with care assessed periodically
- Pharmaco-economic indicators evaluated on an ongoing basis
- Whole exome sequencing typified
- Personal cell line established

In their talk “Herbs and Oils: What's the Latest,” **Dr. John Mark** and **Russell Wise, Pharm.D.**, discussed the ongoing search for complementary therapies to accompany traditional CF care and reviewed three

unique cases to highlight some of the challenges faced when considering complementary therapies. Children differ from adults in their bodies' absorption, distribution, metabolism and excretion of some substances. Few studies have been done in children investigating dietary supplements, and even fewer for treating CF-related problems. How are these products metabolized, and how do they interact with CF medications? Different health care beliefs and practices exist. Openness and sensitivity are required of caregivers when incorporating alternative health care approaches.

Information about commonly known essential oils and supplements like Indrepta C formulated with curcumin and frankincense, horse chestnut, doTerra Respiratory Blend, and eucalyptus oil was reviewed in the context of uses and claims when managing symptoms and treating CF. Wise gave a brief overview of how the FDA review and approval of dietary supplements and drugs differs. With billions of dollars in sales, thousands of products, and thousands of emergency department visits in the United States every year attributed to adverse events related to dietary supplements, officials and public health experts have become concerned about unsafe ingredients in supplements.

The FDA recently launched a tougher oversight of supplements. Wise suggested the following: Be aware of supplement safety, and consult with specialists for advice before using complementary therapies. Be alert for these red flags: big promises and advertisements that label a product as having a “secret ingredient,” or being a “miracle cure,” “scientific breakthrough,” “ancient remedy,” or “revolutionary discovery.” Beware of pseudomedical jargon. Although terms such as “purify,” “detoxify” and “energize” sound impressive, they are generally used to cover up a lack of scientific proof.

Beware of cure-alls, whereby the manufacturer claims that the product can treat a wide range of symptoms or cure or prevent a number of diseases, and remember that testimonials and anecdotes

from individuals who have used the product are no substitute for scientific proof. Also, guarantees and limited offers are used to get you to buy before you can evaluate the product's claims.

### Afternoon session

#### Pediatric session

**Julie Matel, RD**, spoke about the importance of achieving maximal growth in children with CF. There is a strong correlation between growth, lung function and overall health in individuals with CF. Matel spoke about the importance of nutritional status early in life and the association with improved lung function and survival in CF. Weight is an important predictor of growth and the development of other CF complications. She discussed dietary interventions to promote optimal weight gain and growth in infants through teens, other medical interventions like growth hormone and appetite stimulants, and how modulator therapies affect growth and weight gain. In summary, growth deficits in CF patients are clinically relevant, and there is a need to understand underlying causes.

Advocating for your child is part of what medical social worker Teresa Priestley does. Her job entails advocacy and developing related resources. She reviewed many of the detailed guides and forms that are available for download and discussed the importance of the partnership with your child's health care providers. The approach is known as family-centered care because doctors have medical expertise, and parents know their child.

**Russell Wise**, pediatric clinical pharmacist and CF pharmacist at Packard Children's, and **Jake Brockmeyer**, pharmacy resident, spoke about their work in research, in the clinic and in the hospital. In their own words, they wear many different hats! Among other things, these pharmacists are involved when there are CF hospitalizations—for example, monitoring drug levels and taking advantage of telehealth.

**Dr. Eric Hamberger** spoke at length about e-cigarette use in adolescents and young adults with cystic fibrosis. After a review of the historical background of these devices, he answered the question "What is an e-cigarette, and what is in one?" He discussed FDA regulation of e-cigarettes, talked about risk perception and use in people with CF, showed slides of the components of this class of devices, discussed the composition of e-liquids, and showed examples of many varieties of e-cigarettes. He discussed nicotine and addiction and the impact of nicotine exposure during pregnancy and adolescence, describing lasting consequences for brain development. And there are compounds aside from nicotine also found in e-liquids.

#### Adult session

**Dr. Ryan Dougherty**, California Pacific Medical Center adult program director, gave a detailed history of the collaboration between Stanford and CPMC in San Francisco, highlighting the many firsts that occurred in San Francisco over the years. The program at CPMC provides ease of transition for pediatric patients at CPMC living in San Francisco. Inpatient services include the following: interventional radiology, ENT, rehabilitation/exercise, microbiology lab, and a palliative care team including nurses who have 20 to 30 years of experience with CF. One of the unique research projects underway at CPMC is the NovaBiotics cysteamine Phase 2 study, which started with a patient inquiry. Outpatient services include an intensive inpatient program (young adults) and, in the future, an adult CF program.

#### For more information about the CPMC adult CF program, contact:

San Francisco Lung and Sleep  
1100 Van Ness Avenue, Suite 1005  
San Francisco, CA 94109  
(415) 923-3421

**Caroline Okorie, MD, MPH**, clinical assistant professor, gave an overview of sleep and specific

factors relevant to patients with CF. Children and teenagers with CF are affected by insomnia and sleep disturbances in high numbers, so it is important to understand sleep. Sleep is an active process with several phases and stages regulated by several neurobiological processes. Sleep is restorative, building muscle and bone, activating the immune system, and consolidating learning and memories. Poor sleep has many causes and can affect all aspects of health.

It can result in low mood, poor learning, decreased immune function, heart disease, hypertension, diabetes, depression, anxiety, overall poor health and lower quality of life. Newer studies also associate poor sleep with increased depression and suicide risk. Common causes of inadequate sleep include electronics, work/school demands and stress.

The list of CF-specific factors affecting sleep also includes chronic cough, musculoskeletal pain, frequent stooling, reflux/heartburn, abdominal discomfort, overnight feeds, medication side effects and respiratory treatments. Studies show that 50 percent of patients with CF report disturbed sleep, and this increases with the presence of severe lung disease and for those awaiting transplant. Chronic pain is reported in most patients with CF, and most patients report that they are self-managing pain. Patients should let the CF team know about pain issues, so that they can help find ways to reduce pain, and a sleep specialist can be of assistance in addressing sleep issues, including insomnia.

**Dr. Vinayak M. Jha**, from the CPMC Adult Cystic Fibrosis Center, spoke about healthy bones in CF. He first described healthy bone anatomy and some of the many functions of the skeleton. A healthy skeleton provides structural support for the rest of the body, permits movement, protects vital internal organs, provides maintenance of mineral homeostasis, and provides the environment for new blood cells to grow within the marrow spaces.

Bones are living, active structures, which undergo remodeling, starting before birth and continuing throughout life. Remodeling allows old bone to be resorbed and new bone to be formed. Most of an adult's skeleton is totally replaced by new bone about every 10 years! Up to 90 percent of peak bone mass is acquired by age 18 in women and 20 in men, so the first 20 years of life are crucial in building up the greatest amount of bone mass.

The bone mass can keep growing until the late 20s, at which point peak bone mass is reached. Different factors affect peak bone mass, such as race, hormones, and nutrition, including having adequate calcium. Peak bone mass tends to be higher in men than in women, with boys acquiring more bone mass after puberty than girls. Calcium deficiencies in young people can account for significant differences in peak bone mass and can increase risk for hip fractures later in life. Boys, girls and young adults who exercise regularly generally achieve greater bone mass than those who don't. Even after 30 years of age, regular weight-bearing and resistance exercise can help prevent bone loss. In terms of lifestyle, cigarette smoking and heavy alcohol use are associated with lower bone mineral density (BMD).

There are different causes of reduced bone mass and bone density in people with CF. Various reports have shown that vitamin D deficiency is common in CF, likely due to poor absorption of vitamin D from the gut and inflammation resulting from infections. Many studies have observed the correlation between low body mass index (BMI) and low BMD. Low physical activity may result from reduced lung function in CF or the time needed for CF treatments like nebulizers and antibiotics.

The result is lower BMD. The delayed onset of puberty, which can happen in some young people with CF, also contributes to a lower bone mineral density. Dual-energy X-ray absorptiometry (DEXA) is a way to measure BMD. The procedure takes about 15 minutes, requires no needles and uses very

little radiation. DEXA is recommended to screen for low bone mineral density up to every five years.

“Lung Transplant for Advanced Lung Disease,” was presented by Laveena Chhatwani, MD, MSc, associate medical director, Adult Cystic Fibrosis Center, clinical assistant professor of medicine.

CF lung disease is progressive, and although great strides have been made over the years in improving pulmonary function in adults with CF, advanced lung disease in CF needs close monitoring, evaluation and discussion of transplant. Early referral to transplant allows time to resolve barriers and provide adequate sharing of information.

Dr. Chhatwani described the development of CFF Consensus Guideline for Lung Transplant Referral, the ISHLT Registry (International Society for Heart and Lung Transplantation), and the role of the CF team. Don't hesitate to refer and speak to your team about transplant in CF.

As another CF Education Day came to a close, the feeling of hope filled the air. The cure for all forms of CF is expected. As scientists continue ever more rapidly to unravel the mysteries of CF's mechanisms, successful treatments can be developed, and we, the CF community, await each new development.

Link for the [2019 CF Education Day slides](#).

Save the date for next year's CF Education Day, March 14, 2020.

## Cystic Fibrosis Parent Advisory Council

The **Pediatric Advisory Council** is a group of concerned parents whose children receive care from the Stanford CF Center, who work in partnership with members of the pediatric CF Clinic Care Team to provide the highest quality of care and service to patients and families.

Do you have suggestions? Comments? Questions? Please don't hesitate to contact Amy Baugh at [abaugh@stanfordchildrens.org](mailto:abaugh@stanfordchildrens.org) or Kirsten McGowan at [kmcgowan@stanfordchildrens.org](mailto:kmcgowan@stanfordchildrens.org). We'd love to hear from you!

# Tips to Support Your Child's Physical Activity and Exercise as He or She Gets Older

— Taylor Lewis, MA, CMT, CSCS, PRT

Children grow up fast. One minute they are crawling, the next minute they are graduating eighth grade and moving on to high school. Before you know it, they are out of the house and off to college. You can only hope, as the parent of a child with cystic fibrosis, that your child does have that opportunity: to drive off to college as healthy as one can be, a dream the CF community strives to see. In order to reach this goal, many things have to fall into place, and one thing that will help is getting your child to participate in physical activities as early as the medical care team will allow. Physical activity and exercise have many benefits, and I want to share three approaches with you that can support your child's physical activity and exercise as he or she grows and develops.

## **Enrich the child's life with many things**

Keep the child engaged in multidirectional physical and mental stimulation throughout his or her life. As your son or daughter grows up, he or she will naturally create stronger interests in certain activities more than others.

Over time, this can start to create postural movement patterns and neuromuscular connections that mirror a particular lifestyle, whether it is an active lifestyle or a sedentary lifestyle (hopefully a combination of both). Including your son or daughter in physically and mentally stimulating activities, like sports or dancing, at an early age is a great way to increase a child's body awareness and to improve muscular strength and endurance—all of which are important components in respiratory function

and overall health. Physical activities also create situations where children get to interact with other children and learn how to problem-solve. This can help improve social and behavioral cognitive function, as well as boost a child's spirits, confidence and motivation to exercise.

## **Family fun**

Get the whole family involved. Integrating fun games at the park, in your backyard, or during a family adventure such as camping automatically increases brainpower and will help improve physical capacity; but most important, it creates time for you and the family to bond. Cystic fibrosis is a battle the whole family fights, and staying united and on the same page is important. Whiffle ball and kickball are two great examples of games you can play at the park or in your backyard that incorporate aerobic and anaerobic endurance, upper- and lower-body coordination, but most of all family bonding. Find an activity that the whole family enjoys, and go have fun. It will be a win for everyone.

## **Make exercise fun and challenging**

Exercising is engaging in physical activity. Exercise is the same thing as physical activity; the only difference is the intentions behind it. Children were built to move. They crawl, climb, roll, fall, stand and walk all over the place. Respiratory muscles are also postural control muscles that control movements of the body in all planes of motions.

Creating and introducing physical activities that challenge the postural control muscles can help increase the muscles' endurance and strength,

which can indirectly help their role as respiratory muscles. Playing hide-and-seek or capture the flag, or kicking a soccer ball at or through a target, can create physical and mental stimulation to help improve overall exercise capacity.

These are only three approaches to help your son or daughter increase or change up his or her physical activity and exercise. Remember that the key is to keep your child physically active as long as he or she can. In order to do that, try to keep it fun and challenging, and make sure to carve out some time to play a family game or have a family

adventure each week. There is nothing better than spending time with the family. In the end, pick what works for you, your family and your child.

Physical activity and exercise needs/desires change as a child grows up, and they should. Let them grow with the child. Movement parallels a child's interests, and you can help supplement that by giving your child options. Keep physical activity and exercise a part of his or her life, as well as your family's life. We all need a strong team behind us, and making it a family activity strengthens the bonds behind it.

---

## Why Transition Matters

– Alicia A. Mirza, MD

It is well known that people with cystic fibrosis are living longer on average due to advances in medical therapies. As teenagers with CF age, they move from their pediatric CF center to an adult center. This is an exciting milestone; however, “graduating” from Pediatrics can also be a scary process. The challenges aren't as simple as just finding new parking; but rather, they are leaving a team of trusted providers and entering into an unfamiliar medical system.

“Health care transition” is the process of preparing for care as an adult. The CF Foundation adult clinical care guidelines recommend that the concept of transition be introduced early and that the timing of transition be individualized. Transfer of care typically takes place around high school graduation.<sup>1</sup> In the United States, the majority of individuals transferring from pediatric to adult CF care do so between ages 18 and 21.<sup>2</sup> This is an important but vulnerable time for any adolescent with a chronic illness. Research has shown that lung function decline can accelerate in young adults with CF.<sup>3</sup> They are also at risk for gaps in care, particularly those who lack health insurance or who

are relocating. Luckily there have been nationwide efforts to improve the transfer processes, and most individuals experience minimal gaps in care.<sup>2</sup>

Because CF is usually diagnosed in childhood, parents are often the ones who initially make appointments, plan airway clearance, give other medications, track symptoms, and manage refills. A big part of preparing for adult CF care is shifting these responsibilities to the youth themselves, which fosters independence and optimizes quality of life. The CF Foundation guidelines recommend that adolescents be gradually given more responsibility for self-care and decision-making and be seen alone during clinic visits.<sup>1</sup>

At the Stanford CF Center all of the pediatric and adult providers want to help our adolescent patients prepare for this transition. Families are given literature about the process by our transition nurse coordinator, Mary Helmers. It's common to hear providers ask young children about their medications and encourage them to learn the names and purposes of the medications. Parents may be asked to leave the room for part

*Continues on page 17*

# CF Word Search

– Alyssa Remulla

A K O C G J O S P Z U P U F S D O D R F T N W E A  
 E Z Q P W Z O A E O S T E A L Y Z Q U N R H P M P  
 Y W I O S I T Z S E L V Q H K M L T S R Y A I Y Q  
 T P T T F Y L G U U A S P M W L N W N M N S V Z J  
 Y Q A I H K M D Q L S F J U X A B A R C F P Z O O  
 Z W B R J R O D W O I Z A C L O Z M R U W K G M R  
 K L I Q E M O D E V V Q D P G O L E R Q N O P L K  
 P K X R O H S M W K I G S T S K A L Y D E C O U A  
 A G D N I U T V Y H O N K B R T E V X D Y B R P M  
 N V A S G I J O E C A Z B U I N L M G E P G X K B  
 C S C G I Y Q S I R I P O C Z O F O H N Y Y U P I  
 R I G T J S I I T S J N I B R X G E N I G C F T S  
 E R V E W C Y G C V Y N U E Z X I Q N L E I P C F  
 L C V C N M N T U V S H T S N I C Y M A R B O T C  
 I X W P N U J M P U Y U P D E O T X L S J Q N C C  
 P R X O L E E Q F O B Z C T B D J O B C M K L V C  
 A A P L D R O F Z L M O Q L S P E K G I T D V O M  
 S J Y Z N O I T A B R E C A X E Y R A N O M L U P  
 E I T I L C D Z W I H E H I A G H K P O R D O Z E  
 T O U O I S T B G B N V F T C H O C V T V L C K P  
 X U I E G A S T R O N O M Y T U B E G R B K S R F  
 R Z N Z J L B Q Y I V J W I U Y Y X B E J I H O C  
 M C M N Y F H A T X X E R H N D M C U P R F E W T  
 Y D X N S U Q J E M Q L T T F W O M U Y X H Y T H  
 K B F Q M I X J D K V L S M N Y R N C H K X Z F Q

- 
- |                     |                   |                          |                        |
|---------------------|-------------------|--------------------------|------------------------|
| Albuterol           | Hemoptysis        | Orkambi                  | Pulmonary exacerbation |
| Azithromycin        | Hypertonic saline | Pancreatic insufficiency | Pulmozyme              |
| Chest physiotherapy | Kalydeco          | Pancrelipase             | Symdeco                |
| Gastronomy tube     | Lung transplant   | Pseudomonas              | Tobramycin             |



*Why Transition...  
continued from page 15*

of the visit in accordance with CF Foundation guidelines. Additionally, the adult and pediatric teams meet quarterly to discuss patients who are close to transitioning and work hard to maintain constant and effective communication.

We continue to optimize how medical information moves from our pediatric to adult CF center.

There are a variety of resources online for families about transition, including the CF transition tool set CF RISE, which is sponsored by Gilead and supported by the CF Foundation. The organization Got Transition™, a cooperative agreement between the Maternal and Child Health Bureau and the National Alliance to Advance Adolescent Health, also has helpful tools. Talk to your CF care team about questions or ideas you have about the transition process at Stanford.

<sup>1</sup> Yankaskas JR, et al. Cystic fibrosis adult care: consensus conference report. *Chest* 2004;125:1S–39S.

<sup>2</sup> Sawicki et al. Risk Factors for Gaps in Care During Transfer From Pediatric to Adult

Cystic Fibrosis Programs in the United States. *Ann Am Thorac* 15(2): 234–240, Feb 2018.

<sup>3</sup> VandenBranden et al. Lung Function Decline From Adolescence to Young Adulthood in Cystic Fibrosis. *Pediatr Pulmonol* 47(2): 135–143, Feb 2012.



Alicia A. Mirza, MD

## Current Research Studies

**Vertex 809-122:** Phase 3 study for children 1 to 2 years of age with the F508 mutations evaluating the safety of Orkambi.

**Vertex 770-124:** Phase 3 study for children less than 1 year old evaluating the safety of ivacaftor.

**Utility of Lung Clearance Index:** LCI study to be done in clinic for pediatric patients.

**STOP 2:** A study designed to standardize the best length of time to treat a pulmonary exacerbation.

**RARE:** Rare CFTR Mutation cell collection protocol (currently for people who have two copies of rare mutations).

**Proteostasis 808-01:** Phase 2 modulator study for adults with at least one copy of F508 mutation.

**TEACH:** Phase 4 study to determine if azithromycin impairs the benefits of tobramycin.

**Be In Charge (BIC):** A pilot study designed to determine if the BIC program strategies (calorie counting / weight outcomes) are feasible and effective.

**MAP:** A pilot study to evaluate the feasibility of a medication adherence intervention encourages adherence to treatment regimens.

*Healthy High Calorie...  
continued from page 8*

- Guacamole and tortilla chips
- Dried fruit (peaches, mangoes, raisins)
- Peanut butter on banana or apple slices
- Sports bars
- Oatmeal cookies and whole milk
- Mini bagels topped with cream cheese

**Tips for helping kids become interested in eating:**

If you have picky eaters at home, these ideas can be helpful.

- Involve kids in grocery shopping, menu planning and cooking.
- Use cookie cutters to create fun sandwich shapes.
- Create faces with food.

**High-calorie shake ideas:** Have a smoothie for a healthy high-calorie snack or after-dinner treat.

**Strawberry Banana and Peanut Butter Smoothie**

- 2 tbsp. full-fat milk
- $\frac{3}{4}$  cup plain yogurt
- 1 banana
- 2 tbsp. peanut butter\*
- 5 large frozen strawberries

1. Place the milk, yogurt, and banana in the blender and blend.
  2. Add the peanut butter and strawberries, and blend everything until smooth.
  3. Makes one serving
- \*Substitute avocado for peanut butter for an alternative.

**Chocolate Peanut Butter Smoothie**

- 1 cup nut milk (e.g., almond milk)
  - $\frac{1}{2}$  avocado
  - 3 tbsp. peanut butter
  - 1 tbsp. cacao powder
  - $\frac{1}{4}$  tsp. cinnamon
4. Blend all of the ingredients in a blender until creamy.
  5. Makes one serving



Strawberry-banana and peanut butter smoothie

# Cystic Fibrosis Center at Stanford

## Lucile Packard Children's Hospital Stanford (Pediatric Care)

**Providers:** Carlos Milla, MD (Director), Sumit Bhargava, MD; My My Buu, MD; Elizabeth Burgener, MD; Carol Conrad, MD; David Cornfield, MD; Michael Tracy, MD; Jacquelyn Zirbes, DNP, RN, CPNP

**Clinic Scheduling** ..... (650) 724-4788

**Clinic and Prescription Refill Fax** ..... (650) 497-8791

**Patient Services Coordinator** ..... (650) 498-2655

**Nurse Coordinator:** Mary Helmers ..... (650) 736-1359

**CF Clinic Nurse:** Liz Beken ..... (650) 736-1359

**Respiratory Therapy** ..... (650) 724-0206

**Nutrition:** Julie Matel ..... (650) 736-2128

**Social Work:** Teresa Priestley ..... (650) 736-1905

**Newborn Screening:** Jacquelyn Zirbes ..... (650) 721-1132

**Pharmacy:** Russell Wise, Pharm.D. .... (650) 724-4788

**Clinical Psychology:** Diana Naranjo, PhD

### For urgent issues:

**Monday to Friday, 8 a.m. to 4 p.m.**

Call the CF Clinic Nurse ..... (650) 736-1359

**After hours and weekends:** Call the main hospital and ask for the on-call pulmonology doctor ..... (650) 497-8000

## Stanford Children's Health Specialty Services – Emeryville (Pediatric Care)

**Providers:** Karen Hardy, MD; Eric Zee, MD; Manisha Newaskar, MD; and Rachna Wadia, MD

**CF Clinic Scheduling** ..... (650) 724-8414

**Clinic and Prescription Refill Fax** ..... (510) 457-4236

**Nurse Coordinator:** DJ Kaley, RN ..... (650) 724-8414

**Respiratory Therapy:** Lorraine MacPhee (Tues–Fri)  
..... (510) 587-9631

**Nutritionist, Dietitian:** Ayah El-Beshbeeshy (Tues & Thurs)  
(leave message with DJ Kaley, RN) ..... (650) 724-8414

**Social Worker:** Cleo Rice-Hodge (Tues, Thurs & Fri a.m.)  
..... (510) 362-7504

### For urgent issues:

**Monday to Friday, 8 a.m. – 4 p.m.**

Nurse line ..... (650) 724-8414

**After hours and weekends:** Call the main hospital and ask for the on-call pulmonary doctor ..... (844) 724-4140

## Stanford Health Care (Adult Care)

**Providers:** Paul Mohabir, MD (Director), Laveena Chhatwani, MD (Associate Center Director), Gundeep Dhillon, MD; Jennifer Cannon, NP; Elika Rad, NP; Meredith Wiltse, NP  
**Backup Providers:** Kelly Johnson, NP; Julie Hoang, NP; Christina Quack, PA; Jenny Christensen, PA

**Adult Clinic Scheduling** ..... (650) 736-5400

**Adult CF Center Fax** ..... (650) 723-3106

**Nurse Coordinators:** Mary Jane Ramil (last name A–K),  
Kati Lebowitz (last name L–Z) ..... (650) 498-6840

**Respiratory Therapy:** Gauri Pendharkar, RCP;  
Fernanda Shukla, RCP ..... (650) 736-8892

**Dietitian:** Michelle Stroebe, MS, RD ..... (650) 529-5952

**Social Work:** Meg Dvorak, LCSW ..... (650) 518-9976

**Social Work:** Kate Yablonsky, MSW ..... (650) 444-6512

**Mental Health Coordinator:** Liza Sher, MD

### For urgent issues:

**Monday to Friday, 8 a.m. to 5 p.m.**

Call the nurse coordinator at ..... (650) 498-6840

**Weekends, 7 a.m. to 5 p.m.**

Ask for the adult CF ghost pager ..... (650) 723-4000

**Monday to Sunday, 5 p.m. to 7 a.m.**

Ask for the on-call pulmonary fellow ..... (650) 723-4000

## Sutter Health CPMC (Adult Care)

**Providers:** Ryan Dougherty, MD (Director), Vinayak Jha, MD (Associate Director); Christopher Brown, MD; Carolyn C. Hruschka, ANP-BC

**Adult Clinic Scheduling** ..... (415) 923-3421

**Adult CF Center Fax** ..... (415) 243-8666

**Nurse Coordinator:** Carolyn C. Hruschka, ANP-BC  
..... (415) 923-3421

**Respiratory Therapy:** Bryan Ellis, RCP, Arthur Pundt, RCP  
..... (415) 600-3424

**Dietitian:** Elena Zidaru, RD ..... (415) 923-3997

**Social Work:** Amy Greenberg, LSW ..... (650) 518-9976

**Mental Health Coordinator:** Amy Greenberg, LSW  
..... (415) 923-3854

### For urgent issues:

**Monday to Friday, 9 a.m. – 5 p.m.**

Call the nurse coordinator ..... (415) 923-3421

**After hours and weekends:** Call and ask for the on-call pulmonary provider ..... (415) 923-3421

## New Pediatric Clinic Staff Member



Please join us in welcoming Laura Banuelos, who is our new office assistant (OAIV) for CF. Laura grew up in Fremont, California, and attended California State University, East Bay, where she received a bachelor's degree in criminal justice. She is enthusiastic, caring, and goal-oriented, and has a passion for helping people. Laura has been in the medical field for 12 years. Her medical experience began in June 2007 in dermatology, and then she transitioned to Stanford Children's Pulmonary, Asthma and Sleep Medicine Center in March 2018.

Laura enjoys spending time with family, going to the beach, going to aquariums, hiking, reading and scrapbooking. She is looking forward to meeting the CF patients and families and working with everyone in the department. Laura will assist the patients and families with any insurance needs and authorizations, coordinate clinic visits with procedures and annual studies, and support the CF RNs. Laura is bilingual. She can be reached at (650) 498-2655.

---

## Newsletter Contact Information

**Editor:** Zoe A. Davies, RN, MS, PNP, CCRC  
**Assistant Editor:** Colleen Dunn, RRT, RPFT, CCRC  
**Research:** Colleen Dunn, Zoe Davies, Sean Ryan,  
Jackie Zirbes ..... (650) 444-6512

Visit our website at [cfcenter.stanford.edu](http://cfcenter.stanford.edu)  
for more information about our center and CF.

To subscribe to this newsletter, please contact  
**Cathy Hernandez** at (650) 724-3474  
or [cathyh1@stanford.edu](mailto:cathyh1@stanford.edu).