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CYSTIC FIBROSIS CENTER NEWS & NOTES

SPRING 2019, VOL. XXXIII

NEWS FROM THE FRONT

Research (Modulators) Update

By Samya Nasr, MD, Director, Cystic Fibrosis Center

Cystic Fibrosis (CF) is caused by a defect in the CFTR gene. Children must inherit two defective CFTR genes — one from each parent — to have CF. That results in over 2,000 mutations, which are divided into six different classes depending on the function of CFTR on the lungs and other organs in the body. Some of these mutations lead to CF by creating non-working or fewer CFTR proteins at the cell surface. The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cells in a number of organs including the lungs. That leads to thick secretions and mucus.

To help improve the function of CFTR at the cellular level, Vertex initiated its CF research program in 2000, as part of a collaboration with the CF Foundation (CFF). This CF research program would work to find medications, called modulators, to correct defective CFTR protein. Since the start of this collaboration, Vertex has developed Kalydeko® (ivacaftor), Orkambi® (lumacaftor/ivacaftor) and Symdeko™ (tezacaftor/ivacaftor and ivacaftor), all of them approved by the FDA and available for people with CF. The latest modulators—VX-659 and VX-445—were both discovered by Vertex as part of this collaboration. Currently, other companies are working on other modulators. All are in the research stage.

In 2012, the FDA approved Ivacaftor (Kalydeco), the first treatment that targets the underlying CF defect. Although this drug is clinically effective for only 5 percent of people with CF, the development of Ivacaftor paved the way for other CFTR modulators that may benefit many more patients.

In 2015, lumacaftor/ivacaftor (Orkambi) combination therapy was approved by the FDA for patients with two F508del mutations (the most common CF mutation). Benefits continued to be observed with longer-term treatment, and it has been associated with a 42 percent slower rate of FEV1 decline. Orkambi benefits about 46 percent of people with CF.

In 2017, a combination treatment with the CFTR modulators tezacaftor (VX-661), the second generation modulator, and ivacaftor (Kalydeco) named Symdeko, was approved for CF patients with two F508del mutations or with one F508del and one residual CFTR function mutation.

Most recently, the next-generation CFTR corrector VX-659, in triple combination with tezacaftor and ivacaftor (VX-659–tezacaftor–ivacaftor), was developed to restore the function of F508del CFTR protein. Two Phase III studies investigating the next-generation corrector VX-659 combination were conducted. The first study included 385 patients aged 12 and older that were randomly assigned to the combination of VX-659, tezacaftor and ivacaftor or triple placebo for 24 weeks. The second study (VX-445) consisted of 111 patients with two F508del mutations who were randomized to treatment with VX-659 or placebo, both in combination with tezacaftor and ivacaftor, with an endpoint of mean change in FEV1. The two studies have the potential to treat up to 90 percent of all people with CF.

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NEWS FROM THE FRONT

Research (Modulators) Update

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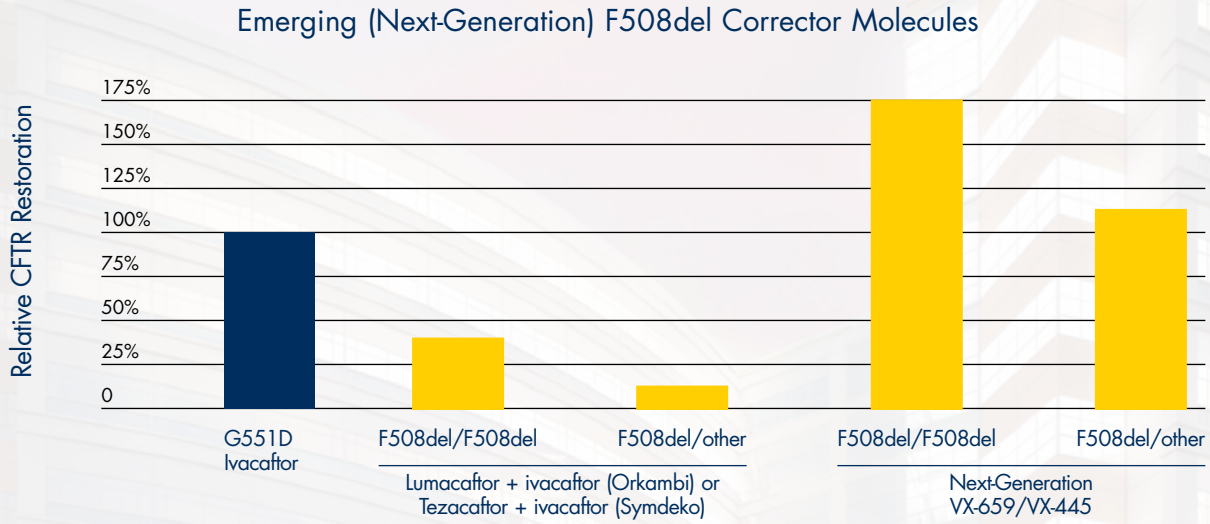


Next-generation F508del correctors promise to be more effective.
Ivacaftor is not as effective at restoring CFTR activity for F508del as it is for gating mutations.

McKenna started Symdeko® in 2018

Vertex recently announced that "treatment with the triple combination of the next-generation corrector VX-659, tezacaftor and ivacaftor resulted in statistically significant improvements in lung function (FEV1) in the 2 Phase 3 studies in people with CF. Data from a prespecified interim analysis of the Phase 3 study in people with one F508del mutation and one minimal function mutation showed a mean absolute improvement in FEV1 of 14.0 percent from baseline at week 4 of treatment compared to placebo ($p<0.0001$). In the Phase 3 study in people with two F508del mutations, the addition of VX-659 in patients already receiving tezacaftor and ivacaftor resulted in a mean absolute improvement in FEV1 of 10.0 percent from baseline at week 4 of treatment compared to the control group in whom placebo was added to tezacaftor and ivacaftor ($p<0.0001$). The VX-659 triple combination regimen was generally well tolerated, and the safety and efficacy from the results supports the potential submission of a New Drug Application (NDA) for the VX-659 triple combination regimen."

Vertex stated that they are evaluating data for the VX-659 and VX-445 triple-combination regimens in the first quarter of 2019 and to choose the best regimen to submit to the FDA for potential approval for people with one F508del mutation and one minimal function mutation.

All patients who complete the two studies, regardless of treatment assignment, are given the opportunity to enroll in a rollover study where all patients receive the VX-659 or VX-445 triple-combination regimen. All patients who had completed the studies at the time of the interim analysis elected to enter the open-label extension study.

The Patient and Family Voice in CF Research

Richard H. Simon, MD, Adult Program Director

The recent successes in developing new CF treatments have been truly amazing. This is particularly true for the CFTR modulators that everyone is familiar with, namely ivacaftor, lumicaftor and tezacaftor…with more on the way. But also under development are new antibiotics, digestive enzymes, anti-inflammatory drugs, mucus clearing treatments, RNA-based therapies and gene editing approaches. When thinking about this collection of treatments, it is reasonable to ask, "Of the many problems caused by CF, who decides which ones are targeted for treatment development?" What usually happens is physicians and caregivers recognize an unmet need and communicate with scientists who work to discover a potential treatment. The decision to move forward needs the support from the laboratory and clinical investigators who run the necessary tests to see if the treatments will be safe and effective. And, of course, there needs to be money to fund the research.

This approach has worked well in the past, but it has become more and more clear that there was an important group of people that was underrepresented in the decision-making process, namely, people with CF and their families. They need to be involved in helping choose and prioritize the research programs. This oversight is now being corrected. People with CF and their families are getting a place at the table when virtually all important research-related decisions are made. Of particular note, the CF Foundation through its Community Voice program provides the means for patients and family members to actively participate in all aspects of CF research. Furthermore, the Foundation has established a subgroup within Community Voice called "Research Voice," whose members have received special training about how research is conducted so they can be even more effective when they participate in the decision-making process.

One of the most significant examples of this trend is the CF Foundation's now-regular survey of people with CF and their families to see what types of research are most important to them. One of the highest priority items that came out of a recent survey is the need to find ways to reduce the treatment burden that people with CF experience every day. It is anticipated that better CFTR modulators may allow some of the older treatments to be discontinued without causing harm. The Foundation is putting forth considerable effort to figure out how to design clinical trials to see what treatments might be stopped. It is safe to say that without input from the surveys, it is unlikely that this line of research would have been given the high priority that it currently has.

The involvement of people with CF and their families is expanding into other types of research activities. Members of Community Voice and Research Voice now sit on many CF Foundation committees that deal with important areas of clinical research. They help decide which grant applications that have been submitted to the CF Foundation will receive funding. They serve on the Foundation's Protocol Review Committees that evaluate all clinical trials that receive Foundation support. The purpose of these committees is to look at every aspect of a clinical trial to make sure that the study is being run in the best possible way. The feedback from people with CF and family members has been very helpful in pointing out features of studies that would make it difficult for someone with CF to participate. A frequent critique is that a study requires too many research visits; also frequently mentioned is that visits as planned last too long. And very importantly, people with CF and family members contribute to the discussion of whether there is an acceptable balance between the risks and benefits from the study.

More recently, the CF Foundation has added people with CF to another part of the research enterprise: as members of data monitoring committees that watch to make sure it's safe for ongoing trials to continue. Traditionally, the committees were composed exclusively of physicians and biostatisticians who are knowledgeable in CF clinical care and research. But the perspective of people with CF was missing.

The assessment of everyone involved in CF research is that the increased participation of people with CF and their families has added an important voice that was previously underrepresented. Anyone interested in learning more about Community Voice and how to participate in the research activities of the Foundation should visit the website at cff.org/Get-Involved/Community/Community-Voice.

COMMUNITY VOICE
CYSTIC FIBROSIS FOUNDATION

WHAT'S NEWS

Respiratory Therapist Clinic Educator

By Sharyn Dagher, BS, RRT

A focus of the CF team is to improve education of our patients and families. All members of the team collaborated to ensure that we were consistent with the information we were sharing with our patients and families. In the early summer of last year, we introduced a new role into the Pediatric CF clinic, that of RT Educator. This new initiative was implemented by having an extra Respiratory Therapist in clinic to focus on education.

During the clinic visit the RT Educator will make contact with patients and their families. It was determined that the approach would be to focus on one topic every quarter, as well as to address any questions or concerns that patients/families may have. Our goal is to help our patients and families be as knowledgeable as possible about their care, to ensure compliance with therapies that will result in improved health.

So far, we have had discussions and education on the proper cleaning techniques of respiratory equipment and proper order of respiratory medications, and we are currently discussing huff coughing technique. These are generally quick topics and aren't meant to increase time in clinic. If more time is needed for education or problem-solving, that can happen after the clinic visit by continuing the conversation in the PFT lab.

Topics that the RT will focus on next include: proper MDI technique, effective airway clearance (correct aerobika/acapella and huff cough technique), recommended cleaning and disinfecting procedures for equipment, proper functioning of equipment (nebulizers and vest) and proper order of therapies. Some of these topics may be discussed when spirometry is being performed. The RT educator in clinic does not replace the yearly Respiratory Assessment that we ask patients/families to participate in. It is important to be able to assess the equipment and ensure that the most up-to-date information has been passed on.

The PFT lab staff is a valuable resource for all our patients and families, and we're always here to help! Please do not hesitate to reach out with any questions or concerns. We can be reached at 734-936-9515.

How can you help improve clinic from your home?

Our CF Center is participating in a national Patient Experience of Care Survey that is supported by the CF Foundation. After your visit in clinic, you may get a call or email about the survey from Quality Data Management (QDM).

Every quarter, the anonymous results are sent to the CF Center so they can review them, looking for areas needing improvement and sharing the results with hospital leadership, if needed. Don't worry: your name (and your child's name) will not be included and you won't be surveyed more than every four months and not more than twice a year.

How does this help? On previous surveys, "time to room patient" was an area that needed improvement in our clinic. This information, coming straight from patients and families through the survey, was then used to help educate and support the clinic as we partnered with administration on ways to fix this problem. Has that helped? Your survey will help show if it has and will aid in future changes!

The survey comprises 30 questions and should only take about five minutes to complete.

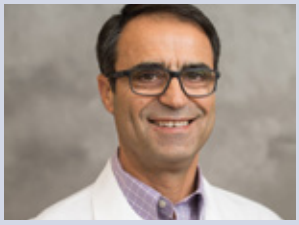
An invitation with a code will come by phone or email.

- **Phone:** call from 440 area code, from Ohio-based QDM.
- **Email:** programsatisfactionsurvey@qdmnet.com (Check your junkmail folder!)

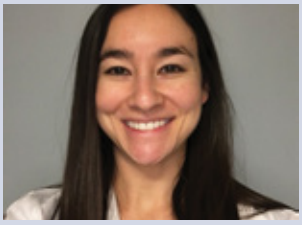
Website: **cff.org/ChildSurvey** (enter code to complete survey)

We want to thank you in advance for your help in making your experience at our CF Center better.

Staff Introductions



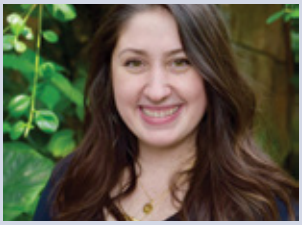
Armando Kurili, BS, CRT evaluates and provides expertise as the Respiratory Clinical Specialist of the adult multidisciplinary clinics: ALS, COPD, CF, Obesity Hyperventilation, and Assisted Ventilation.



Danielle Taylor, MS, RDN, CNSC was an inpatient dietitian in Seattle, WA, but now works with adult CF patients admitted to the medicine critical care unit or with the medicine pulmonary team.

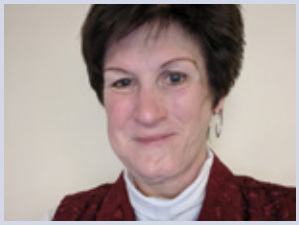
Valerie Nolt, PharmD is a General Pediatrics Clinical Pharmacist Specialist responsible for patient care related to the pediatric pulmonary, endocrine, genetics, and hospitalist services.

Carolyn Faut, MS, RD, CNSC is a clinical dietitian who has taken care of adult CF patients in the CCMU and now continues their care in 8D and on the floor.



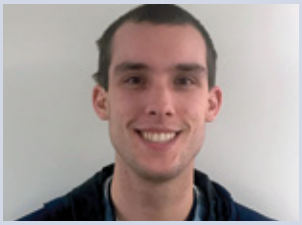
Haley Moraniec, LLMSW studied family and children's services in graduate school. Before joining the pediatric CF care team, Haley worked as a children's therapist at a community mental health agency.

Erica M. Blount, CPhT, BS in Chemistry previously worked in the research pharmacy as a senior pharmacy technician. She joined the research team in 2018 as a clinical subject's coordinator.



Mari Pitcher, MSW, MBA has joined the adult CF clinic and specializes in grief, trauma and patient and family centered care for individuals, and their families, with life changing illnesses.

Amanda Compton, RN, BSN is a registered nurse in the pediatric pulmonary clinic. She previously worked in the PICU at Children's Hospital of Michigan and in the NICU at Emory in Atlanta.



Adam Wojtys, PCTA, joined the Pediatric Cystic Fibrosis Clinic in early 2019. He looks forward to meeting all the patients and families in clinic. His father and two sisters also work in healthcare.

PATIENT SPOTLIGHT

I'm Going to Laugh Anyway

By Christa Kuck

"I know I shouldn't like the way you sound," my roommate told me, "but you sound just like my aunt." I was doubled over laughing, reading a comedy memoir. And I was a few months into an exacerbation that wouldn't get better. I sounded just like her aunt, a lifelong smoker.

For as long as I can remember, I have loved to laugh. I love the laugh that squeezes at my core, brings water to my eyes and leaves me breathless. For me, the intersections of breath and laughter have been many and varied. Laughter has been a powerful force in my life, building me up when I have felt broken down; giving me moments of lightness in times that feel all too heavy.

> *"I don't want to live out my life in sadness, I want to live out my life in joy."*

I was diagnosed with cystic fibrosis when I was 19 years old, in February of my sophomore year of college. The wonderful doctor who finally told me was the eighth physician I had been to, and I was desperate at that point for someone to tell me why my body was falling apart. Why I couldn't stop coughing, why my stomach hurt all the time, why I had lost 14 pounds in as many days. I had an answer that wasn't asthma and allergies, wasn't irritable bowel syndrome, wasn't acid reflux. It was an answer that accounted for all my body's "quirks" that I had long ago discounted.

That time after my diagnosis—and the four years since—have had a lot in them that isn't funny. Telling all my loved ones, and continuing to have to tell new people I meet, that I have a chronic disease is heartbreaking, awkward and occasionally feels like banging my head against a wall. Being diagnosed a year and a half ago with diabetes, another chronic disease, seems just plain unfair. Accepting a new identity for myself—one that includes having a chronic disease, needing a giant vest to stay healthy, taking 20 pills a day—is sometimes sad. Dealing with worry that spirals out of control every time I get a cold is exhausting.

But I don't want to live out my life in sadness, I want to live out my life in joy. So I laugh. I laugh because I have breath and that's a miracle. I laugh because I was born with CF and born a giggler, and I can't change either of those. I laugh because it makes me feel like I'm in control of how I'm feeling. I laugh because there's power in saying I'm going to laugh anyway. I'm going to laugh in spite of.

So, in spite of CF, in spite of diabetes. In spite of exacerbations and antibiotics. In spite of finger pricks, vibrating vests, nebulizers and pill bottles. In spite of pain. In spite of worry. I'm going to laugh. Even when I sound like a lifelong smoker.

Q & A with Sharon Tischio, a CF Parent

Tell us about your son.

His name is Valentino, which means brave or strong. He was diagnosed with CF when he was 3 months old. He is now almost 14 years old and in 8th grade. He is an only child. He has two copies of delta F508 mutation. At 5 months old he was diagnosed with a milk protein intolerance, so he cannot have any dairy. Last year, he was diagnosed with Hashimoto's thyroiditis (hypothyroid) and CFRD.

Valentino started a new school in 7th grade and has truly blossomed. He is loved and respected by his principal, teachers and classmates, and there is an amazing doctor on staff, too! Valentino has kept his disease private at his new school due to some negative experiences in the past. His health is doing pretty good right now, which I attribute to his strict compliance with treatment, medication, stamina and, of course, his love of sports. He is active in baseball, soccer and hockey/ice skating. He learned to play the trumpet and is looking forward to transitioning to marching band next year. He does well academically. He is witty and has a kind spirit.

What are some challenges you both have faced?

Our challenges have included bullying, people not understanding CF and a lack of support to help manage daily life. Valentino choosing not to share his disease with his peers has created challenges, too. He is challenged with being mindful of nutritional needs and caloric intake, which is especially important since his CFRD diagnosis. He has lost some weight recently due to neglecting his supplement shakes for snacks at school. Starting hockey without having extra caloric intake has also contributed. During baseball and soccer, he had some serious sugar lows as the insulin dose was being adjusted. That was a big stressor for both of us.

Were his sports team supportive during those times?

Yes. The CFRD diagnosis was a bittersweet one. I noticed that most people actually took his health challenges seriously. They asked many questions, including how they could help. Valentino's baseball coach stopped an All-Star game to check his blood sugar. However, I've never seen anyone mention good cough hygiene. CF is such an invisible disease, but they do know diabetes.

How do you manage it all?

As a CF mom I must be organized, mindful and well rested. I have to constantly plan ahead to the best of my ability. I have to know and plan around school schedules/ functions, weather forecasts, sports, etc. I always carry medication, food and enzymes at all times to allow for flexibility in our daily lives. I order medications and food supplements well in advance to avoid the stress of possibly running out.

"I don't want to look back on my life and say 'I wish I would have.'"

How do you find time for yourself?

The one thing that I do for myself is to make sleep a priority. My goal of 7.5-8 hours of sleep each night is mandatory for me to function efficiently. Without proper sleep, I find it difficult to complete everything correctly and plan appropriately. Another thing I make time for is helping others, especially others with CF. It is good therapy for me. I have served on the Mott CF Family Advisory Board and currently volunteer for the Bonnell Foundation. It brings me strength to help others.

How do you see your mentoring and kindness to others impact Valentino?

I think it impacts him so positively. I live by example showing him that helping other people is good medicine for body and mind. That impact of kindness to others and from others physically on Valentino is so amazing to experience. It is an experience of how mental health impacts your physical health positively.

What do you want to tell CF patients and families?

To live in the moment and to be mindful. To enjoy the calm when you're able to. Know that there are always rough seas ahead. I would also tell them to continually educate themselves about CF and advocate for those with CF. Lastly, I would tell them to be present and to simplify life if possible. I don't want to look back on my life and say "I wish I would have." I realize that I won't get a second chance. Live passionately. The body and mind will adapt. Our only option living with CF is to not give up, you must go forward.

TEAM UPDATES

Pediatric Family Advisory Board Update

By Catherine Enochs, BSN, RN, AE-C, Pediatric Program Coordinator

The Pediatric Cystic Fibrosis Family Advisory Board (FAB) has been busy again this year. Our advisors are instrumental in improving our CF Center. They share patients' and families' experiences in order to help drive quality improvement in our clinic and hospital.

Looking at different ways to connect with families, the FAB has started several new ventures. First, a FAB newsletter is being created, which will become a quarterly communication with families. Our advisors are also maintaining a Facebook page specifically for our CF parents. This creates an easy line of communication to the board members. Projects can be communicated to our CF community and patients or families can post concerns or questions to board members. This allows the FAB to represent all our CF patients and parents more thoroughly.

Join the private Pediatric FAB Facebook group at **facebook.com/groups/AnnArborCFfab**

In addition, one of our FAB members was able to join our Quality Improvement Project for improving FEV1 in our patients. She worked hard and contributed much to the project. At the North American Cystic Fibrosis Conference, she talked with other CF Centers at the QI Fair, where we showcased our work as a team.

We're looking forward to 2019, when we plan to add more board members and find new areas of improvement to focus on.

Adult Patient Advisory Board Update

By Katie Hall, LMSW, Adult Program Coordinator

Our Patient Advisory Board has been meeting monthly to discuss ways to make our center as great as it can be. Our group meets using a platform called BlueJeans where we can all see/interact with each other online. The Advisory Board's Mission is to ensure the highest standards of comprehensive and compassionate healthcare. We do this by collaborating with our entire healthcare team to strengthen communication and collaboration among patients, families, caregivers and staff and promote patient and family advocacy and involvement.

The Advisory Board brought to our attention the difficulty in trying to coordinate appointments with CF/GI/Endocrine clinics, and we have been able to create a solution. Now, at checkout, you can ask to have all these appointments scheduled for the same day! We're also currently working on making a magnet that will list symptoms so patients will know when to contact the care center vs. when to go to the ER. Be on the lookout for these to be distributed in clinic in 2019!

If you are interested in joining our Advisory Board, please reach out to Katie Hall at **734-998-6067** or email **aultkath@med.umich.edu**.

CFPEERCONNECT

CF Peer Connect is a peer mentoring program for people with cystic fibrosis and CF family members age 16 and older. Through this program, you'll be matched with a peer mentor who has experience with topics that are important to you. Together, you can connect over video, phone or email. Visit **cfpeerconnect.com/about.**

Want to securely email your doctor?

Sign up for the My U of M Health Portal. Your U-M labs and tests can be reviewed via this portal. You can send messages to your doctor, nurse, dietitian or social worker; request refills; and even reschedule appointments, all via the secure patient portal. Visit **myuofmhealth.org** to get your access code and sign up! *(Please note: The Portal should not be used for sick calls.)*

How to Care for Your Pelvic Floor

By Kristin Keith, MS, PT

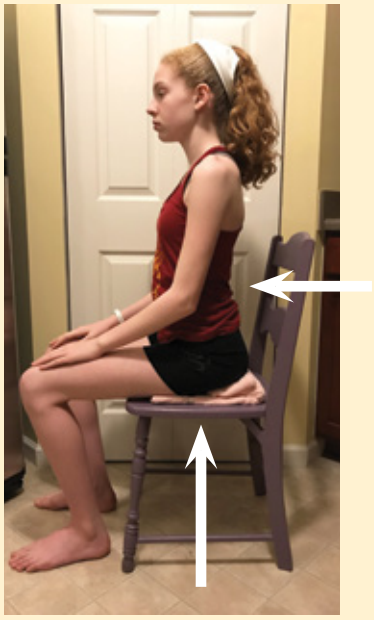
The pelvic floor muscles are a group of muscles that make up the bottom (or "floor") of the pelvis. They support the organs in the pelvis and form a sling around the rectum and vagina. Having the proper balance of strength and the ability to relax the pelvic floor muscles allows for the controlled passage of urine and feces. The excessive coughing and increased abdominal strength found in people with cystic fibrosis can lead to weakness or difficulty allowing the pelvic floor muscles to work correctly. This may lead to incontinence.

The rate or prevalence of incontinence in young people with CF ranges from 18 percent to 47 percent in girls, and 2 percent to 9.4 percent in boys. The prevalence of incontinence in women with CF over age 18 can be as high as 74 percent. The goal of physical therapy is to reduce the rate of incontinence in young people with CF and stop its progression. Prevention is ideal, but improvements can be made if a problem already exists. To address prevention or improvement, we need to work on reducing the pressure in the belly.

Three ways to reduce the pressure in your belly:

1. Practice diaphragm breathing. When you breathe in, the belly should move out.
2. Don't hold your breath! When you lift a weight or a bag of groceries, even when you get up out of bed, be sure to breathe out during the action. Blow out as you perform the activity.
3. Perform your airway clearance sitting upright, feet on the floor, so the diaphragm and pelvic floor muscles can work in rhythm together.

These activities can become part of a regular routine without adding more "exercises" to an already busy day. Please discuss any questions or concerns with your physical therapist during your next outpatient clinic visit.



No slouching, with lower back straight.

Great Strides 2019

Great Strides provides a fantastic opportunity for family, friends, students and colleagues to come together and make a difference. Each year, more than 125,000 people participate in over 400 walks across the country! The event harnesses the power of people with a shared vision and encourages collaboration, team building and leadership as we take steps to find a cure for cystic fibrosis.

Your participation in Great Strides matters a lot! We don't just want to treat CF. We want to end CF. Register now at **cff.org/greatstrides**

GREAT STRIDES®

CYSTIC FIBROSIS FOUNDATION

Great Strides is coming to a city near you!

SATURDAY, MAY 4, 2019
Toledo, OH

SUNDAY MAY 5, 2019
Detroit, MI
Kalamazoo, MI

SATURDAY MAY 11, 2019
Ann Arbor, MI
Davison, MI

SATURDAY MAY 18, 2019
Grand Rapids, MI
Auburn Hills, MI

SUNDAY MAY 19, 2019
Findlay, OH
Grand Haven, MI
Remus, MI

FRIDAY MAY 31, 2019
Petoskey, MI

SATURDAY JUNE 1, 2019
Frankenmuth, MI

SATURDAY JUNE 8, 2019
Port Huron, MI
Mount Pleasant, MI
Lansing, MI

RESEARCH UPDATES

The CF Foundation's Therapeutics Development Network (TDN) is a driving force in CF research. Michigan Medicine is a CF Therapeutic Development Center, which allows us get involved in clinical research so we can contribute to making improvements in CF treatments and therapies. However, we can only accomplish that with the participation and help of our patients. One of the research team will be available in the clinics to introduce ongoing studies to you and answers any questions you might have. If you have questions about our research program, you may contact Marisa Linn at **mlinn@med.umich.edu** and Dawn Kruse at **dmkruse@med.umich.edu.** If you are approached about participating in a study, we encourage you to give it a try.

In order to help you better understand some of the studies open to enrollment, below are brief summaries of research we are conducting at Michigan Medicine.

Antibiotic Studies:

1. TEACH: Adding Chronic Azithromycin to Inhaled Tobramycin to determine whether azithromycin reduces the benefit of inhaled tobramycin by comparing changes in pulmonary function **(recruiting ages 12 years+)**
2. SAV005-04: Inhaled Vancomycin for the treatment of MRSA **(recruiting ages 6 years+)**
3. STOP2-IP-15: Standardized Treatment of Pulmonary Exacerbations II to determine the optimal duration of IV antibiotic treatment **(recruiting ages 18 years+)**
4. STAR-ter: cycled antibiotics for eradication of new cases of MRSA **(recruiting ages 2-45 years old)**

Anti-inflammatory Studies:

1. APPLAUD: Use of LAU-7B to reduce inflammation in adults **(recruiting ages 18 years+)**

Enzyme Studies:

1. CF-FC: Fibrosing Colonopathy in US Patients with Enzymes **(recruiting)**

Behavioral Intervention Studies:

1. Project UPLIFT to Reduce Anxiety and Depression in CF Patients: determining the effectiveness of telephone- or web-based group mindfulness and cognitive behavioral therapy in patients with depression or anxiety **(enrolling ages 13+)**

Modulator Studies:

1. PTI-428-06: Use of PTI-428 in adults with two copies of the F508del mutation who are taking Symdeko **(recruiting ages 18+)**
2. PTI-801-01: Use of PTI-801 with PTI-808 or Symdeko **(recruiting ages 18+)**
3. PTI-808-01: Use of PTI-808 alone and in combination with PTI-801 and PTI-428 in patients with two copies of the F508del mutation **(recruiting ages 18+)**
4. VX14-661-110: VX-661/Ivacaftor combo, 12 yrs and older, 1 or 2 copies of DeltaF508 **(enrollment closed)**
5. VX17-659-102: VX-659 Combination Therapy, DeltaF508 and a Minimal Function Mutation **(enrollment closed)**
6. VX17-659-105: VX-659 Combination Therapy, 1 or 2 copies of DeltaF508 **(enrollment closed)**

Observational Studies:

1. CHEC-OB-17: CFTR Modulated Changes in Sweat Chloride and Outcomes- for patients currently taking an FDA-approved CFTR modulator **(enrolling all ages)**
2. PICC: evaluating the factors influencing PICC line problems during treatment of CF exacerbations with IV antibiotics **(enrolling ages 6+)**
3. NTM-OB-17: Evaluation of a standardized approach to diagnosis (PREDICT) and treatment (PATIENCE) of nontuberculous mycobacteria (NTM) **(enrolling ages 6+)**
4. DESIGN CF Phase II: Developing e-Health Systems to Improve Growth and Nutrition in CF **(enrolling parents of CF patients ages 3-12)**
5. PROMISE: evaluating the effects of CFTR modulators on airway inflammation and microbiology **(enrolling ages 12+ soon)**
6. GOAL-e²: G551D Observational Study – Expanded to Additional Genotypes and Extended for Long Term Follow-Up **(enrollment closed)**
7. BARRIERS: Standardizing Measures of Barriers to Treatment Adherence **(enrollment closed)**
8. The EPIC Observational Study: Impact of Pseudomonas aeruginosa Acquisition and Early Anti-Pseudomonal Treatment in Children (Years 11-15) **(enrollment closed)**

Allergic Bronchopulmonary Aspergillosis

By Amy Filbrun, MD, MS, Associate Director, CF Center

Allergic bronchopulmonary aspergillosis, or ABPA, is a lung problem that is caused by an allergic reaction to Aspergillus, a type of fungus or mold. Aspergillus is found everywhere in the environment. It is in soil, dust, water, dead leaves, dried grasses, hay, and marijuana, to name just a few. The fungus forms spores, small particles that float in the air and that get in our lungs when we breathe. Many people have Aspergillus in their airways, but most are able to clear the spores without difficult; and exposure causes no harm. This is usually called "colonization." However, people with a weakened immune system are at risk for Aspergillus to invade the lungs and cause an acute and serious infection. And in people with cystic fibrosis or asthma, exposure to Aspergillus triggers an allergic immune response without causing an invasive infection in the lungs.

Colonization with Aspergillus is common in CF, and is seen in 5 to 60 percent of patients with CF. Only a small portion of these patients will develop ABPA (1-20 percent). It can be challenging to diagnose ABPA in patients with CF, as many of the symptoms are common to CF as well. Therefore, a high index of suspicion is necessary.

Symptoms of ABPA include:

- Increased cough
- Increased sputum production, with sputum most often being a grey/brown color
- Wheeze or bronchospasm
- Exercise intolerance
- Decrease in lung function

** Persistence of all the above despite usual treatment for CF (including treatment for an exacerbation)*

Allergic bronchopulmonary aspergillosis is diagnosed by a combination of factors, including a poor response to routine CF care, new changes on chest x-ray, very high levels of IgE (the immune system's response to allergens), positive skin test or aspergillus specific IgE and aspergillus IgG (antibody). Cultures for aspergillus may be positive or negative, neither of which rules out ABPA. There are also other molds that can cause this type of response, although they are less commonly encountered.

Once diagnosed, treatment for ABPA is aimed at reducing the inflammatory response to Aspergillus to prevent injury to the lungs. First-line treatment is oral corticosteroids, such as prednisone or prednisolone. These are anti-inflammatory medications that block the allergic response. Generally, treatment with oral corticosteroids requires a long course, tapered over months. Inhaled steroids alone do not tend to be effective for management of ABPA.

The second line of therapy is anti-fungal medication. These medications, such as itraconazole or voriconizole, help to kill Aspergillus so it no longer lives in the airway. This treatment is not curative, as we are continually exposed to aspergillus, so recolonization is common. Both of these lines of treatment have been successful in improving symptoms and leading to remission. However, both can have significant and long-term side effects. Newer treatments are being evaluated and used. These include the use of anti-IgE injections, known as omalizumab, which is an antibody that attaches to your IgE antibody and binds it to prevent the allergic reaction. Finally, as a way to avoid the long-term side effects of ongoing oral steroids, very high dose pulse steroids given intravenously have been used successfully, usually starting at three days each month, and tapering over time.

If ABPA is not controlled with treatment, it can lead to lower lung function and damage to the airways. This leads to damage in the lung (central bronchiectasis), which in turn leads to more pooling of secretions and ongoing symptoms and damage. Research is being done to further evaluate treatment options, including the use of anti-IgE therapy, best use of anti-fungal medications, early detectors of ABPA and what triggers ABPA, to help understand why some people develop it but others do not.

If you'd like more information on ABPA, there is an excellent webcast on the CFF website at **cff.org/Life-With-CF/Daily-Life/Germs-and-Staying-Healthy/What-Are-Germs/Aspergillus-and-Allergic-Bronchopulmonary-Aspergillosis**. Also the American Thoracic Society has a nice patient information handout at **thoracic.org/patients/patient-resources/resources/allergic-bronchopulm-aspergillosis.pdf**.

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