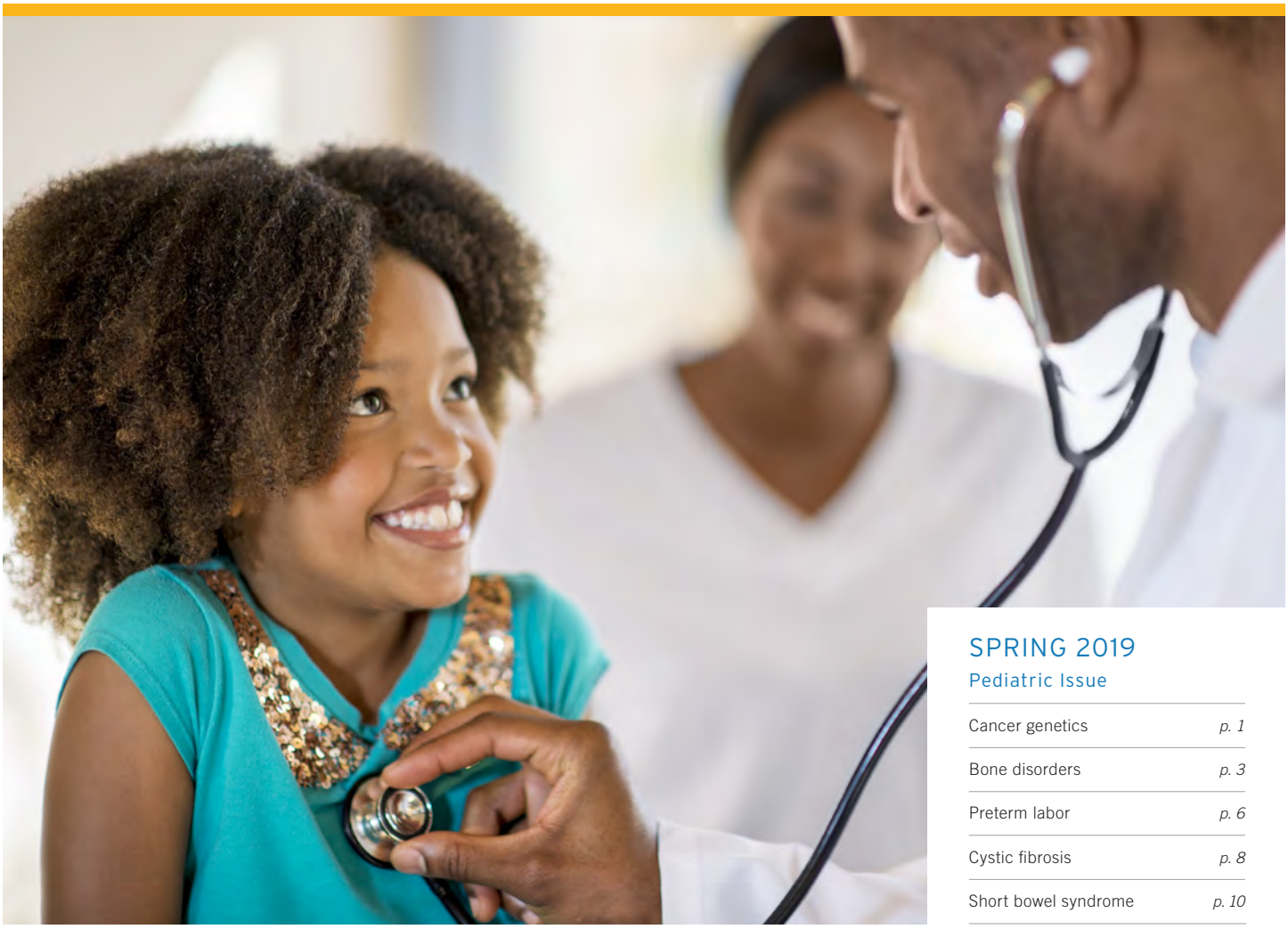
UCLA Health | it begins with U

Physicians Update



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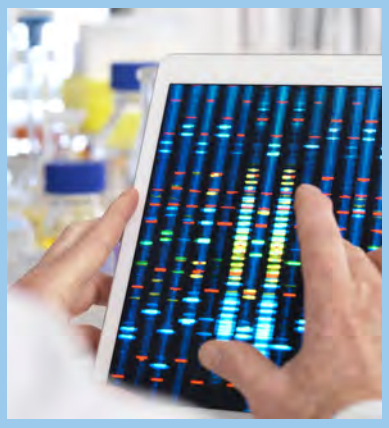


GENETICS

Center works to identify children with genetic predisposition to cancer

A pioneering clinic at UCLA Mattel Children's Hospital is making a significant impact on the lives of children and their families with rare genetic conditions that predispose them to cancer, as well as those diagnosed with pediatric cancers that are potentially related to a rare genetic syndrome.

The UCLA Pediatric Cancer Predisposition Clinic was established in 2012, at a time when powerful new genetic testing technologies were first being implemented clinically at UCLA. This so-called next-generation DNA sequencing enabled, for the first time, comprehensive testing of all of

continued on p. 4

UCLA Clinical Updates

Learn about the latest advances from UCLA

Clinical study to improve scleroderma lung disease outcomes

UCLA pulmonologists and rheumatologists are leading a nationwide clinical trial comparing two medication regimens in treating pulmonary fibrosis in scleroderma patients. The investigation will help determine if the anti-fibrotic drug pirfenidone can improve outcomes when paired with the current standard of care — the immunosuppressive agent mycophenolate.

Evidence supports wider use of transcatheter aortic valve replacement (TAVR)

Design advances and continuing clinical investigation are expanding the use of TAVR. Originally approved for aortic stenosis patients who were not considered candidates for open valve-replacement surgery, the percutaneously placed valve is now approved for use in patients who are at intermediate risk for open surgery.

Fighting pediatric epilepsy with the ketogenic diet

A randomized, controlled trial in children with daily seizures in spite of multiple failed medication trials demonstrated that the ketogenic diet was associated on average with an almost 40 percent reduction in seizure frequency, with some patients experiencing a greater than 90 percent seizure reduction or seizure freedom.

Children who have seizures despite medical therapy may be candidates for epilepsy surgery

Epilepsy surgery is highly successful in carefully selected children with medically refractory seizures, but remains an underutilized option. Surgery is no longer considered an extreme or "last-resort" option for seizure control. In some cases, early epilepsy surgery may be the best method to maximize children's developmental and cognitive potential.

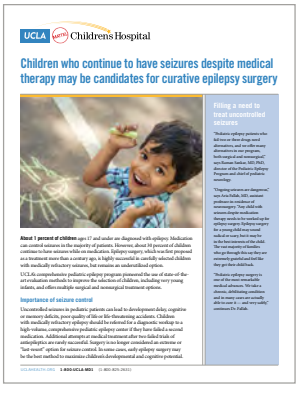
To download these and other clinical advances at UCLA Health, go to:
uclahealth.org/clinicalupdates


UCLA Mattel Children's Hospital

Fighting pediatric epilepsy with the ketogenic diet


UCLA Health

Evidence supports wider use of transcatheter aortic valve replacement


UCLA Mattel Children's Hospital

Children who continue to have seizures despite medical therapy may be candidates for curative epilepsy surgery

News from UCLA Health

Teens who volunteer and engage in civic life are healthier

High school teens in California who volunteer, take part in community aid groups, and join school or other clubs are healthier and more likely to aspire to attending college, according to a study by the UCLA Center for Health Policy Research. The study found that regardless of race or family income, one-in-three teens have a high level of civic efficacy, defined as caring about issues, feeling connected to others who are engaged in civic activities and feeling as if they can make a difference.

uclahealth.org/teenvolunteers

Fractures, head injuries common in e-scooter collisions

UCLA researchers have found that people involved in electric scooter accidents are sometimes injured badly enough — from fractures, dislocated joints and head injuries — to require treatment in an emergency department.

uclahealth.org/scooterinjuries

New clues about what goes awry in brains of people with autism

A team of UCLA-led scientists has discovered important clues to what goes wrong in the brains of people with autism — a developmental disorder with no cure and for which scientists have no deep understanding of what causes it. The new insights involve RNA editing — in which genetic material is normal, but modifications in RNA alter nucleotides, whose patterns carry the data required for constructing proteins.

uclahealth.org/autismclues

Specialized center offers evaluation and treatment for perplexing bone disorders

Bone disorders — from fragile bones that easily break to diseases that affect mineral metabolism and cause bone deformities or conditions resulting in short stature — can diminish a child's quality of life and often are perplexing to clinicians. But a specialty program at UCLA Mattel Children's Hospital, the Pediatric Bone Program, offers a multidisciplinary team approach, including pediatric orthopedic surgeons, geneticists and dentists in the evaluation and treatment.

"This is a field in which you need a team of experts, and that is the benefit of practicing in a major center such as UCLA," says program director Isidro B. Salusky, MD, a pediatric nephrologist and a leader in the field of bone and mineral abnormalities in patients with chronic kidney disease and rare genetic bone disorders.

Among the conditions seen at the program's clinic are childhood osteoporosis and fractures, osteogenesis imperfecta, hypophosphatemic rickets, pseudohypoparathyroidism and tumor calcinosis, as well as poor bone mineralization from disordered phosphate, calcium and vitamin D metabolism. Some patients have bone problems due to chronic conditions and immobilization, such as seizure disorders or cerebral palsy. Children with chronic kidney disease and other chronic conditions can experience complications, such as bone deformities, short stature and fractures. Post-organ transplantation, (kidney, liver and heart) patients also can develop osteoporosis and fractures, and such disorders may persist. Still others are referred because they are experiencing idiopathic fractures with minimal trauma.

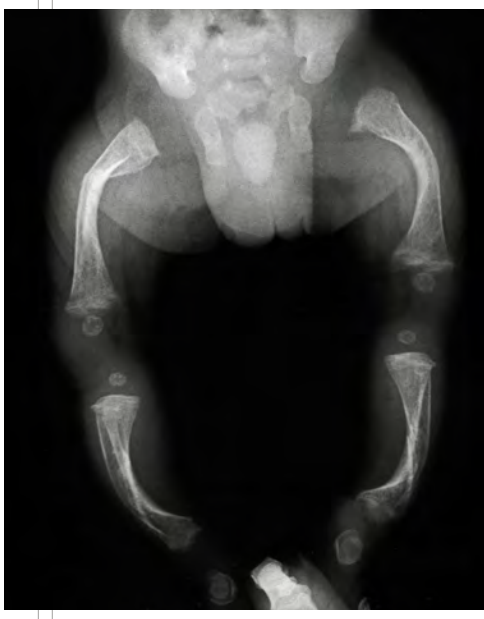
"We see a wide variety of conditions, some of which have a genetic basis, and others that develop over time or are secondary to medications or other chronic medical diseases," says Katherine Wesseling-Perry, MD, a pediatric nephrologist on the program's medical team. "We evaluate the full spectrum of disorders."

The evaluation process begins with a history and physical exam, including specific blood tests, and often includes dual-energy X-ray absorptiometry (DEXA) scans to measure bone mineral density or more sophisticated bone density tests for children with growth delay, Dr. Wesseling-Perry explains. Blood tests assessing calcium phosphate, vitamin D nutrition and other biomarkers help to determine if a problem with mineral metabolism is contributing to the disease, and further lab tests also can be ordered to determine the cause of bone fragility.

For cases that continue to defy diagnosis, UCLA is among the few centers in the country that is qualified to perform and interpret bone biopsy through a sophisticated technique in which a small piece of bone is removed from the iliac crest and sent to the bone histomorphometry laboratory for analysis. "Through both traditional bone histomorphometry and immunohistochemistry, we learn about the basic pathology of bone and see how specific proteins are expressed at the bone level, and whether or not they have a role in the disease pathogenesis," says Dr. Salusky, who heads the lab.

Effective treatments are available for most bone disorders, Dr. Wesseling-Perry notes. One of the most exciting new therapies to become available in recent years is an antibody to the fibroblast growth factor 23 (FGF23) molecule, a highly effective new therapy for patients with bone mineralization disorders, such as hypophosphatemic rickets.

"Sometimes, especially in the case of fractures, the lines can be blurred between what's normal and what might be pathological," Dr. Wesseling-Perry says. "In general, any concern about excess fractures, bone deformities, bone pain or a chronic condition requiring medications that can impair the bones should be referred to a specialized center for evaluation."



X-ray of osteogenesis imperfecta (OI), or brittle bone disease. OI is a genetic disorder that causes the bones to break easily.

Image: Science Source

For cases that continue to defy diagnosis, UCLA is among the few centers in the country that is qualified to perform and interpret bone biopsy through a sophisticated technique in which a small piece of bone is removed from the iliac crest and sent to the bone histomorphometry laboratory for analysis.

COVER STORY

Center works to identify children with genetic predisposition to cancer

STORY HIGHLIGHTS

A pioneering clinic at UCLA Mattel Children's Hospital is making a significant impact on the lives of children and their families with rare genetic conditions that predispose them to cancer.

The UCLA Pediatric Cancer Predisposition Clinic brings together oncologists, geneticists, genetic counselors and social workers to provide diagnostic genetic testing and counseling, as well as personalized screening protocols as needed.

(continued from cover)

the protein-coding regions of the genome to diagnose rare conditions and identify genetic predispositions.

"At the time, little was known about the utility of genetic testing in children with genetic syndromes that could predispose them to early cancers," says Julian A. Martinez, MD, PhD, a clinical geneticist and the center's codirector. "We believed it had potential value in that it would enable surveillance of patients with these predispositions to detect and treat the tumors early, as well as facilitating targeted treatments in patients already diagnosed with cancer based on the genetic cause identified."

That initial vision has borne out, Dr. Martinez notes, and the clinic's approach to patients with cancer-predisposing genetic conditions or cancers resulting from genetic syndromes has become the international standard for how such patients should be evaluated and managed. The clinic's value has only grown with the continued advances in DNA sequencing technologies and the development of new treatments that target the specific genetic mutations underlying an individual patient's cancer.

"With our state-of-the-art genetic testing, we can put an end to the diagnostic journey so that these families are no longer making their way through the medical system, trying to find answers. We are able to provide a medical home for these patients and a roadmap for what to expect, in addition to better-informed treatment."

The UCLA Pediatric Cancer Predisposition Clinic remains one of the few multidisciplinary efforts of its kind, notes Vivian Y. Chang, MD, MS, a pediatric hematologist-oncologist and codirector of the clinic. The clinic brings together oncologists, geneticists, genetic counselors and social workers to provide diagnostic genetic testing and counseling, as well as personalized screening protocols as needed. All cases are discussed at a weekly genomic board meeting that includes bioinformatics specialists and pathologists, as well as clinicians.

Most of the clinic's patients fall into one of two categories. The first are those who have already been diagnosed with a genetic syndrome associated with a high risk for developing a cancer. "My role as the oncologist is to educate these patients about their cancer risk and develop personalized cancer screening plans," Dr. Chang explains. "We know that if we catch these cancers early, it offers the best prognosis and the best treatment options. We can now utilize targeted treatment for patients who are identified to have specific genetic mutations, whereas in the past, we had no specific treatments or we used broad-stroke chemotherapy and/or radiation to kill cancer cells. This is how we envision personalized medicine in the future for everyone."

Dr. Chang has been a leader in developing surveillance guidelines for patients with underlying genetic syndromes that predispose to cancer risk, as part of an expert panel convened by the American Association for Cancer Research. "With these genetic diagnoses that are this rare, it's important to share data across centers," she notes. "By doing so, we have developed evidence-based guidelines so that these patients can be treated in a standardized way."

Image: Science Photo

The second major population of patients seen at the clinic are children — and in some cases, adults — who have already been diagnosed with a cancer, but certain features of their presentation or family history suggest an underlying genetic cause. Often, Dr. Martinez notes, these patients have gone through what is commonly referred to as a diagnostic journey, presenting with multiple medical conditions that have eluded a unifying diagnosis. "With our state-of-the-art genetic testing, we can put an end to the diagnostic journey so that these families are no longer making their way through the medical system, trying to find answers," Dr. Martinez says. "We are able to provide a medical home for these patients and a roadmap for what to expect, in addition to better-informed treatment."

Ending the diagnostic journey brings multiple benefits, Dr. Martinez notes. For families, there is great psychological benefit to finding closure after a long, emotionally trying odyssey in search of an explanation for their child's symptoms. That journey can include expensive and ultimately fruitless testing, at significant cost to both the families and the health care system. In some cases, the definitive diagnosis points to a condition that could affect other family members, who can then benefit from being tested and, if they test positive, being treated or more frequently screened, as appropriate.

Dr. Martinez says that roughly 10 percent of the pediatric cancer patients referred to the clinic have been found to have a well-documented genetic syndrome, and his team has described new syndromes along the way. Other centers that have followed the UCLA clinic's approach have found, similarly, that about 10 percent of their pediatric cancer patients will have a known genetic disorder that can benefit from surveillance and personalized care.

Roughly 10 percent of the pediatric cancer patients referred to the clinic have been found to have a well-documented genetic syndrome.

Image: Getty Images

STORY HIGHLIGHTS

A UCLA Mattel Children's Hospital research group is making significant progress in preclinical studies of a drug that could significantly reduce the risk of preterm labor in women with intrauterine infection or inflammation.

Antibiotic drugs fail to sufficiently address infections in the womb because they target only the microorganisms responsible for the infection but not the inflammation that results from the immune response, leading UCLA researchers to explore ways of targeting the inflammation itself.

Drug study aims to reduce risk of preterm labor in women with infection in the womb

Nearly one-in-10 births in the U.S. are premature — before 37 weeks of pregnancy — putting the child at increased risk for infant death, long-term health problems and developmental delays. After declining from 2007 to 2014, preterm birth rates in the U.S. have risen slightly in the last several years, according to the U.S. Centers for Disease Control and Prevention. But a UCLA Mattel Children's Hospital research group is making significant progress in preclinical studies of a drug that could significantly reduce the risk of preterm labor in women with intrauterine infection or inflammation, which is believed to be the causative factor in about 40 percent of preterm labor cases.

Suhas Kallapur, MD, the UCLA neonatologist who heads the research team, explains that these cases of infection and inflammation are unlike traditional infections, in that they aren't typically associated with symptoms such as fever, vomiting or diarrhea. "In many of these women, we can't find the organisms that are causing this problem, but the infection or inflammation appears to be localized to the womb," Dr. Kallapur says. "That's why it can be so silent in many

cases. However, the consequences are not benign." In addition to the risk of preterm labor, he notes, when the womb is infected it exposes the fetus to this inflammatory insult, which can cause problems with the developing organs.

Antibiotic drugs fail to sufficiently address the problem in the womb, Dr. Kallapur explains, because they target only the microorganisms responsible for the infection but not the inflammation that results from the immune response. Instead, his research group began looking for ways of targeting the inflammation itself. Several years ago, Dr. Kallapur's group embarked on a systematic effort to understand the mechanisms that lead to the inflammatory response within the womb as well as the hierarchy of these inflammatory molecules, hypothesizing that an immunomodulatory approach could then target the inflammation using an anti-inflammatory drug already on the market.

For their studies, Dr. Kallapur and colleagues at Cincinnati Children's Hospital, in collaboration with the California National Primate Research Center at UC Davis, developed an animal model using the rhesus monkey, and found that by injecting certain agents that induce either infection or inflammation in the intrauterine cavity, they could create chorioamnionitis — a condition found in the placenta of about half of all women who deliver at less than 28 weeks. "By studying human placenta and modeling this condition in animals, we created a chorioamnionitis model in which all of the conditions we see in humans are mimicked," Dr. Kallapur says.

Based on the research of other groups, Dr. Kallapur suspected that the pro-inflammatory cytokine interleukin-1 (IL-1) is a major culprit in the intrauterine inflammation. To test that hypothesis, his group used the biologic drug Anakinra, which prevents IL-1 from attaching to its receptor and thereby causing the downstream inflammatory effect. In addition to being commonly used for rheumatoid arthritis, Anakinra is frequently prescribed for women, including pregnant women, who have joint problems, inflammatory bowel disease or psoriasis.

Sure enough, Dr. Kallapur's group reported in the *Journal of Clinical Investigation Insights* in 2018 that the drug has significant beneficial effects of reducing inflammation at the maternal-fetal interface. Previously, the group, collaborating with colleagues, found that Anakinra reduces inflammation resulting from chorioamnionitis in the fetus. While both the studies were in rhesus models of chorioamnionitis, the data are very encouraging that IL-1 is an effective therapeutic target for both mothers and babies exposed to chorioamnionitis and its associated morbidities.

The research remains in the preclinical phase, but Dr. Kallapur is hopeful that these studies will pave the way for clinical trials targeting two populations of pregnant women: those who have preterm membrane rupture, which substantially increases the risk of infection; and women who experience idiopathic preterm labor. "If we can safely prolong delivery by one-to-two weeks, or even a few days, that could have an important impact on survival of the baby, as well as on the side effects from being exposed to the infection," Dr. Kallapur says. The National Institutes of Health recently funded Dr. Kallapur's lab at UCLA to conduct additional preclinical studies of safety and efficacy of Anakinra.

"The inflammatory effects on the fetus have lifelong implications," Dr. Kallapur says. "Neonatal mortality is one of the major indicators of health status of a country, and among western industrialized countries, the U.S. is near the bottom by that measure. That is driven to a large extent by prematurity. This is a major public health problem that needs to be addressed, and we are encouraged by the results of our preclinical studies."

"If we can safely prolong delivery by one-to-two weeks, or even a few days, that could have an important impact on survival of the baby, as well as on the side effects from being exposed to the infection."

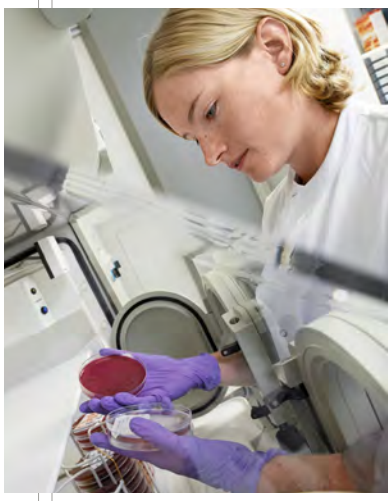
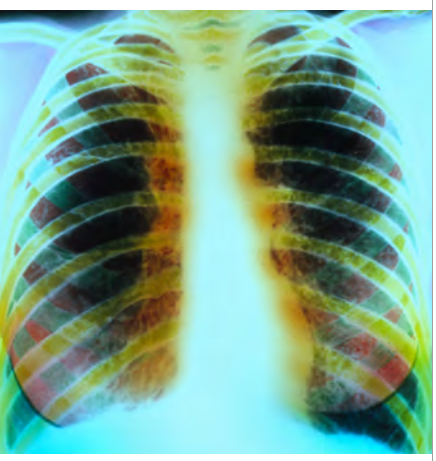


Photo: Science Source

New therapies lead to major advances in treatment of cystic fibrosis

A new class of drugs designed to correct genetic mutations that cause cystic fibrosis (CF) has dramatically improved the outlook for those patients who have the specific mutations targeted by the drug therapies, say the codirectors of the UCLA Mattel Children's Hospital Cystic Fibrosis Center, which recently was accredited as a Core Center by the Cystic Fibrosis Foundation.



Colored chest X-ray of the lungs of a patient with cystic fibrosis. Bones, such as the ribs around the lungs, are green. Within the lungs the bronchial walls (orange) beside the spine (down center) have thickened due to repeated infection. The diaphragm (blue, lower center) is low because of airway obstruction.

Image: Science Source

STORY HIGHLIGHTS

Nearly half of CF patients can benefit from one of the two currently available cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies.

Previous treatments have addressed life expectancy, but the new therapies treat the underlying cause of the disease.

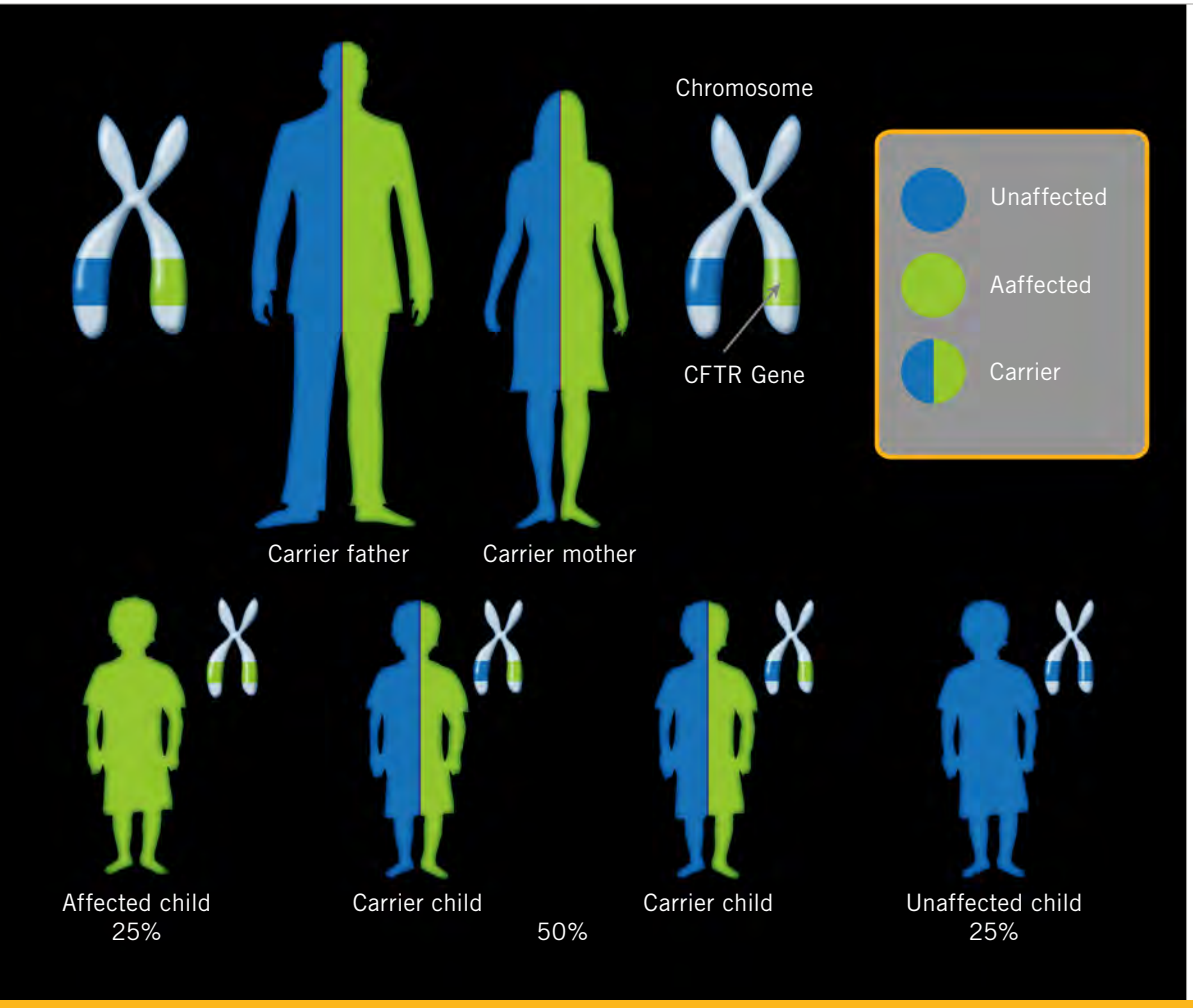
Pediatric pulmonologists Marlyn S. Woo, MD, and Douglas Li, MD, note that nearly half of CF patients can benefit from one of the two currently available cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies, which target the malfunctioning protein encoded by the CF gene, which regulates the flow of water and chloride in and out of cells in the lungs and other organs. A third CFTR modulator therapy, currently awaiting approval by the U.S. Food and Drug Administration (FDA), would expand the proportion of CF patients eligible for CFTR modulator therapy to approximately 90 percent.

"Before these CFTR modulator therapies, we could only symptomatically treat CF patients with drugs to help them with malabsorption or to thin the thickness of the airway mucus," Dr. Woo says. "But we couldn't really go after the source of the disease, which is the dysfunction of the CFTR protein. Now we have directed therapy."

Dr. Li notes that the CFTR modulator therapies have a beneficial impact on lung function, as well as decreasing pulmonary exacerbations and weight gains. "These are typical end points we look at in CF, and there are fairly substantial improvements in all of those based on recent data," Dr. Li says. "Previously, we had made large strides in life expectancy by mitigating the end-organ effects of CF. What's exciting about these new therapies is that, for the first time, we are able to treat the underlying cause of the disease."

CF is a progressive, inherited disease that causes persistent lung infections and gastrointestinal/liver disease in affected patients. Approximately 30,000 people have been diagnosed in the United States, the majority of them before age 2. There is no cure, but the outlook for children who are diagnosed has improved dramatically. In the 1950s, the median survival age for CF patients was 2. As recently as the early 1980s, it was only 14. That began to change dramatically with newborn screening to detect the disease early, mechanical therapy to loosen thickened mucus and help patients expel it from their lungs, improved antibiotics, nutritional enhancement and digestive enzymes. By 2016, according to CF Registry data, the median predicted survival was 47 years — a jump from 41 the previous year, thanks to the introduction of the first-generation CFTR modulator therapies. More than half of the CF patient population is now older than 21. "This is no longer a pediatric disease," Dr. Woo says.

The CFTR modulator therapies are designed to correct the mutations that impede the primary function of the CFTR protein — to restore function of a channel for chloride (a component of salt) to flow across the cell surface. When the CFTR protein is not made correctly, it causes an imbalance of salt and fluids inside and outside the cells, leading to thick, sticky mucus in the lungs, pancreas and other organs. When proper chloride flow is reestablished, the mucus becomes rehydrated. More than 1,700 mutations



Cystic fibrosis. Diagram showing the genetic disease cystic fibrosis transmembrane conductance regulator mutation (CFTR) in humans and within the inheritance patterns of their offspring.

Image: Science Source

in the CFTR gene have been identified, some of them common and others extremely rare.

The first such medication, ivacaftor, was approved in 2012 for patients with at least one copy of the CF mutation G551D. While the drug markedly improved the pulmonary function of patients with the mutation, it was indicated for only about 4 percent of CF patients. More recently, though, a combination therapy — ivacaftor and either lumacaftor or tezacaftor — was approved for patients with two copies of the most common CF mutation, DeltaF508, which accounts for some of the most severe lung diseases in CF patients.

In addition, Dr. Li notes, the FDA has used data from in vitro studies to expand indications for the new drugs so that they can treat a wider range of mutations, and a recently developed process called theratyping, which matches medications with mutations, will enable more patients with rare mutations to benefit from the modulators. Moreover, if, as expected, new triple-drug modulator therapy is approved by the FDA, combining the three CFTR modulators, approximately 90 percent of CF patients will be eligible to benefit.

"This is the closest therapy we have had to a cure, and soon we hope to be able to successfully treat all CF patients," Dr. Li adds. "We want them to all be able to lead full and healthy lives, free of this disease."

"Before these CFTR modulator therapies, we could only symptomatically treat CF patients with drugs to help them with malabsorption or to thin the thickness of the airway mucus. But we couldn't really go after the source of the disease, which is the dysfunction of the CFTR protein. Now we have directed therapy."

Children with short bowel syndrome benefit from recent treatment advances

Recent advances have vastly improved the outlook for children with short bowel syndrome, a life-threatening disease characterized by loss of intestinal length and function resulting in the inability to absorb sufficient nutrition within the gut, say two UCLA Health experts who are part of a multidisciplinary team that manages patients with the condition.

STORY HIGHLIGHTS

Short bowel syndrome is the most common cause of intestinal failure in pediatric patients.

UCLA's comprehensive program features a multidisciplinary team with expertise and experience to manage the most complex cases and ensure that children achieve optimal growth and development.

Short bowel syndrome — also referred to as short gut syndrome — is the most common cause of intestinal failure in pediatric patients, notes Robert S. Venick, MD, a pediatric gastroenterologist at UCLA Mattel Children's Hospital. "It can develop in utero through conditions such as intestinal atresia or gastroschisis, or more commonly in the early postpartum phase, often in premature babies from conditions such as necrotizing enterocolitis — in which a portion of the intestine becomes ischemic and requires surgical resection," he explains. "As a result, these children become dependent on intravenous nutrition to sustain life."

UCLA is a nationally and internationally recognized center of excellence for the care and rehabilitation of patients with intestinal failure, with one of the highest-volume programs and excellent outcomes. The comprehensive program features a multidisciplinary team consisting of gastroenterologists, neonatologists, registered dietitians, clinical nurse specialists, social workers, pediatric surgeons and transplant surgeons, all of whom have the expertise and experience to manage the most complex cases and ensure that children achieve optimal growth and development. Because short bowel syndrome and other causes of intestinal failure have lifelong implications, adults as well as children are treated at the center, which provides long-term continuity of care.

For patients with short bowel syndrome, total parenteral nutrition (TPN) is a life-saving therapy. A central venous catheter is placed, and a liquid solution containing glucose, protein, fat and essential vitamins and minerals is infused directly into the patient's circulation — typically on a daily basis over a period of several hours. "In the short run, TPN is needed to prevent dehydration and electrolyte or salt imbalances," explains Kara L. Calkins, MD, a UCLA Mattel Children's Hospital neonatologist who is part of the intestinal failure center team. "And in the long term, particularly for children, it's needed to sustain appropriate growth and development." At UCLA, a team of experts closely monitors patients on TPN to ensure that they aren't developing any adverse complications and that they are growing properly, Dr. Calkins notes. There is often a need to adjust the nutrition or administer medications to promote better intestinal absorption; in some cases, pediatric surgeons are needed for staged surgical procedures.

"Decades ago, short bowel syndrome was seen as a death sentence. Today, if children survive the acute process when they first become ill, many of those who are treated on an ongoing basis by an expert team at an intestinal failure center will do very well, with a good quality of life."

This 8-month-old baby girl was born prematurely and has suffered from gastroschisis. Gastroschisis is an abdominal wall defect in which the intestines or other organs protrude outside the fetus. In this case, the outer protruding section of intestine was removed surgically, a procedure that resulted in short bowel syndrome.

Image: Science Photo

For the vast majority of children with short bowel syndrome, the intestine grows to the point that they can be weaned off TPN. "Our goal in the care of all of these children is over time to allow their remnant small bowel to undergo the process we refer to as intestinal adaptation, in which they eventually can receive all of their calories through their GI tract," Dr. Venick says. "We know that the intravenous nutrition is life-sustaining, but both for quality of life reasons and because it can be associated with significant complications, our goal is to use TPN as a bridge to get them to full enteral autonomy."

The length of the intestinal adaptation process can range from months to years, Dr. Venick adds. UCLA is participating in clinical trials of new medications aiming to hasten the process. In the rare cases when children with short bowel syndrome are unable to be weaned from TPN or face significant adverse consequences from the disease, they may need to be considered for an intestinal transplant, an area of medicine in which UCLA is also an international leader.

One of the main concerns for any patient who is dependent on long-term TPN is the infection risk that comes with having a permanent IV inserted into a large vein, but Dr. Calkins notes that in recent years, efforts to prevent and promptly treat central line-associated bloodstream infections have led to significant improvements. A second major concern is that although IV nutrition is life-sustaining, it has the potential to damage the liver. That problem has been greatly reduced with changes in the IV fat provided to patients — from soybean oil, which is known to be toxic to the liver, to fish oil, which is more protective.

"Decades ago, short bowel syndrome was seen as a death sentence," Dr. Calkins says. "Today, if children survive the acute process when they first become ill, many of those who are treated on an ongoing basis by an expert team at an intestinal failure center will do very well, with a good quality of life. Thanks to new therapies, new surgeries and new nutritional strategies, the outcome for these children has changed dramatically, even over the last 10 years."

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Front cover photos: Getty Images