Cystinosis MAGAZINE

SPRING 2012

FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION

History in the Making
The Path to Approval
Special Kids, Special Lessons
The G-Tube Question

Currently, there is no cure for cystinosis,

but there is hope.

Cystinosis is a rare, inherited, metabolic disease that is characterized by the abnormal accumulation of the amino acid cystine in each of the body's cells. Build-up of cystine in the cells eventually destroys all major organs of the body including the kidneys, liver, eyes, muscles, bone marrow, thyroid and brain.

Medication is available to control some of the symptoms of this insidious disease, but cystinosis remains incurable.

Cystinosis afflicts approximately 500 people, mostly children, in North America and fewer than 2,000 worldwide. It is one of the 7,000 rare or "orphan" diseases in the United States that collectively affects approximately 30 million Americans.

Federal funding for research on cystinosis and other rare diseases is virtually non-existent and most pharmaceutical companies remain uninterested because financial rewards are too small.

Yet, while there is only a small number of patients who suffer from any given "orphan" disease, knowledge gained by studying one disease often leads to advancements in other rare diseases and more prevalent and well-known disorders.

Cysteamine, currently the medicine used to treat cystinosis patients, is also in clinical trials as a possible treatment for Huntington's disease and NASH (fatty liver disease), which affect millions of people worldwide.

The Cystinosis Research Foundation was established in 2003 with the sole purpose of raising funds to find better treatments and ultimately a cure for cystinosis.

Today, CRF is the largest provider of grants for cystinosis research in the world, funding more than 92 studies and fellowships in nine countries.

CRF has raised nearly $18 million, which it has granted or committed to cystinosis research studies around the world. CRF's efforts have changed the course of cystinosis research and given new energy to its investigators and scientists.

CRF's commitment to research has given hope and promise to the global community of cystinosis patients and their families.

CYSTINOSIS
RESEARCH FOUNDATION

For more information about the Cystinosis Research Foundation, call 949-223-7610 or visit www.cystinosisresearch.org.

18802 Bardeen Avenue, Irvine, CA 92612-1521

On the front cover: Addison Cox and Tina Flerchinger
Cover photo by Lars Wanberg

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Cystinosis Magazine is printed on recycled paper.

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To receive our monthly e-newsletter, *Star Facts,* send your email address to zsolsby@cystinosisresearch.org.

The entire cost of *Cystinosis Magazine* is underwritten by friends of the Cystinosis Research Foundation.

Cystinosis Research Foundation website www.cystinosisresearch.org

Dear Friends and Family:

Spring has arrived yet again and with it the hope and promise of new life and new beginnings. I am struck by the sense of optimism we are surrounded by as a result of the remarkable progress CRF researchers have made over the past year. 2012 promises to be another exciting year as we eagerly anticipate FDA approval of RP103, the delayed-release medication and approval of the first stem cell treatment for cystinosis.

I hope you are as excited as we are about the continued progress and new discoveries CRF-funded researchers and scientists have made. Since 2003, CRF has funded over 92 research studies and fellowships leading to novel treatments, new therapies and new discoveries about the fundamental science of cystinosis. In this issue of *Cystinosis Magazine,* you will find an update on the new medication and you will meet Dr. Ranjan Dohil, the CRF-funded researcher who discovered the delayed-release medication. We also have a feature article on Dr. Julie Ingelfinger, a CRF Scientific Review Board member who shares her perspective on the breadth and scope of CRF research. What sustains this community from the harsh realities and daily life with cystinosis is the hope and promise of better treatments and a cure for cystinosis. It is all about research.

Photo by Lars Wanberg

In 2003, we funded our first research study. Today, thanks to the leadership and guidance from our brilliant Scientific Review Board members, we issue new research grants and fellowships twice a year ensuring that the cycle of research continues and thrives. On average we fund more than $2 million in grants every year. We continue to focus on translational research in an effort to initiate clinical trials for new therapeutic treatments for cystinosis.

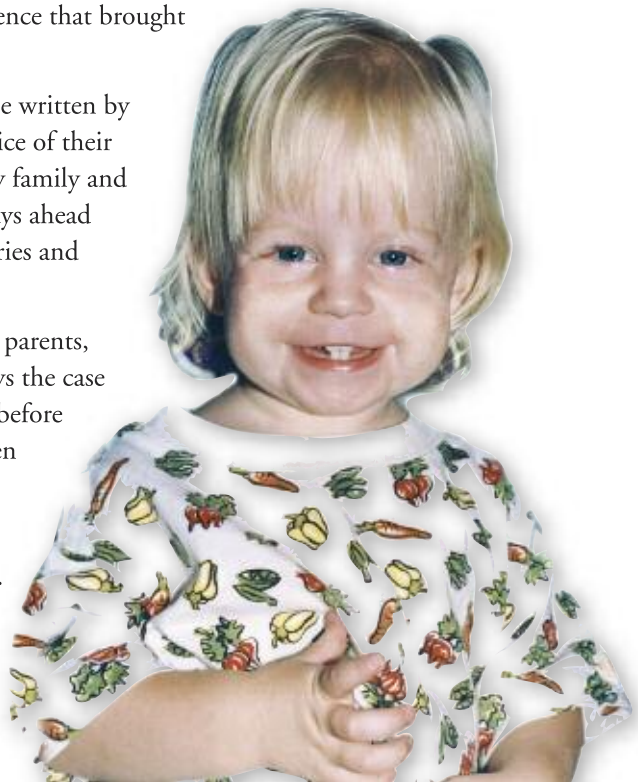
CRF recently hosted the Third CRF International Cystinosis Research Symposium for CRF-funded researchers and scientists at the Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering in Irvine, California. A major objective of the meeting was to accelerate research and encourage collaboration between the 60 scientists who presented their data and shared new research ideas and discoveries.

The contagious energy and enthusiasm of the CRF science community and a strong sense of camaraderie were evident throughout the two-day conference that brought many friends and colleagues together again.

I am moved beyond words when I read the stories in this magazine written by cystinosis families and patients who open their hearts to share a slice of their daily life with cystinosis. What resonates is the sense of hope every family and patient has and their strong conviction that there will be better days ahead for those diagnosed with cystinosis. There is resilience in their stories and so much optimism about what tomorrow will bring.

Natalie turned 21 years old in February – for most celebrants and parents, it is a time of independence and true adulthood. That is not always the case when a loved one is affected by a disease like cystinosis. The days before Natalie's birthday were emotional and led to some honest and open discussions about life and cystinosis.

Natalie's health is slowly deteriorating – she has pain in her eyes, her muscles are weakening and fatigue is her constant companion. Now that she is older, her care is completely her responsibility.



She is doing an amazing job of keeping up with the demanding medication schedule. Generally, her spirit is remarkably and blessedly high, which allows her to transcend many of the challenging health issues she faces. However, before her birthday in February, she confided that she did not want to turn 21, that she was afraid of the future, afraid of dying. We held her as she sobbed and said that she wanted to be a mother and wife someday but she was afraid that she might not live long enough to experience those life milestones.

We promised her that she would realize her dreams. We asked her to stay strong, keep her faith and trust that progress is being made every day by cystinosis researchers and scientists. It was painful for us to know that on her 21st birthday, she was worried about dying instead of thinking about how much life she has ahead of her. Instead of feeling carefree and liberated, she was worried and fearful about what tomorrow would bring. These are new fears, new struggles – this is life with cystinosis. Until there is a cure, there is no cure. Cystinosis wreaks havoc on her body and now taunts her usually optimistic spirit and outlook on life.

Recently Natalie called to tell me that she had been at the bookstore in Georgetown and had purchased two books. I asked what the titles of the books were. She stated that they were books to read for pleasure. She then said coyly, "I don't think you are familiar with the first book; it is called, *Men are from Mars, Women are from Venus."* She was surprised when I said, "Yes, I have heard of that book!" We had a good laugh! I then asked what the title of the second book was and she said, *"The Stem Cell Hope."* Silence – my heart broke – what 20-year-old buys a book on stem cells? It was a sobering moment for me – our young adult daughter wanted to learn more about love and relationships and at the same time, sought to learn more about what will save her life. I wanted to get on the next plane, hold her and hug her and tell her that we won't let her down – we are on the right path to the cure.

This year marks our 10th CRF *Natalie's Wish* event – it is certainly a special year as we celebrate our research community, our family, our friends and the milestones we have reached as a foundation. We have been blessed with your support, love and friendship – each and every one of you are the reasons we are successful.

As we live this next chapter of life with cystinosis and its new challenges, we are even more grateful for your love, support and friendship. You have lifted us up and gifted us with your dedication to the cystinosis community. Together we will find a cure for cystinosis.

With blessings from our family to yours,

Nancy, Jeff, Alex and Natalie

A NOTE FROM NATALIE

Dear Friends and Family:

I am a junior at Georgetown University in Washington D.C. this year and college life has been treating me well! This semester I live in an on-campus apartment with three other girls; it was a change for me, but I really enjoy living with other people. I like the camaraderie and the company.

Currently I am taking four courses and my favorite class this semester is Abnormal Psychology. I just found out that I was accepted into a summer program in France. I will be living with a French family and studying French in Tours, France. I hope to develop and perfect my French-speaking skills and integrate myself into the French culture. Living abroad for seven weeks will be quite a challenge, but I am very excited to live there for the summer.

This year, I turned the big 21 years old! I celebrated with my family in Las Vegas where we saw some great shows and had a fantastic time together. I am so happy that I am finally "of age"! Turning 21 is a huge milestone, and for me, it means that yet another year has gone by living with cystinosis – a successful year I might add.

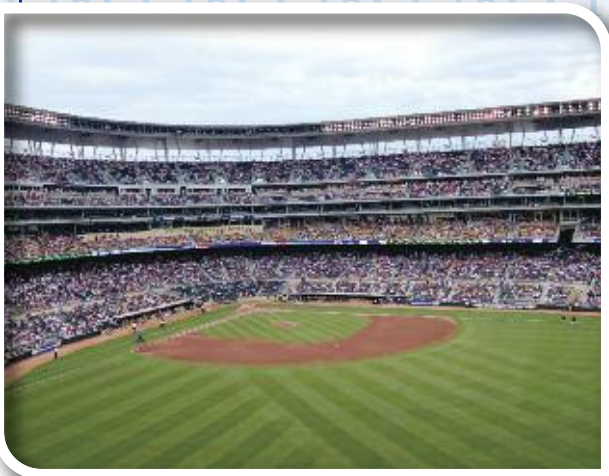
Even though turning 21 was wonderful, it does make me think more about my future and my health. It is scary knowing that as I get older, my body is deteriorating a bit more each day.

I am now more dedicated and committed to taking the eye drops because I am worried that if I don't, I will go blind. For me, going blind is the scariest part of cystinosis. Each day is a struggle, but I have learned to take one day at a time and focus on the positive aspects of my life rather than the negative ones.

Although cystinosis can be very overwhelming, I know that there is hope for a cure and hope that all of us with cystinosis will live better and longer lives.

Love, Natalie

CCIR Update



BUILD IT AND THEY WILL COME

By Betty L. Cabrera, CCIR Curator

In this update, I wish to share insight as to the vision that led to the creation of CCIR.

VISION

Those who have followed the articles about cystinosis research in this magazine and/or other sources know that innovative scientists are hard at work in the laboratory looking to develop new and improved therapies. Eventually, some of these projects will move further down the research pipeline to test potential therapies in human clinical trials.

At this stage of research, progress relies largely on the availability of two resources that only cystinosis patients can provide:

1. Information about the impact of the disease and their experience with existing treatments, and
2. Their own voluntary participation as human subjects in clinical trials.

In anticipation of meeting these research needs, medical experts and cystinosis family organizations collaborated to establish the first-ever online patient registry for cystinosis.

CCIR was created and launched in late August 2010 for the express purpose of streamlining the collection of these resources and hastening the pace of progress.

CCIR CURE CYSTINOSIS INTERNATIONAL REGISTRY

The hope was – to borrow and adapt a catch phrase from the popular 1989 baseball fantasy film *Field of Dreams* – "Build it and they will come." The film's story line also happens to be fitting analogy for the vision behind CCIR and its current success.

In short, the movie tells how a small farmer constructs a baseball field amid the corn rows in Iowa and precipitates the convening of history's most beloved baseball heroes to play ball games that draw spectators from miles away. In the same vain as the film, the idea behind building a dedicated patient registry was that those everyday heroes who champion against the detrimental health effects of cystinosis would assemble in one place, rallying together to beat cystinosis and live better and longer lives.

Enrollment in CCIR allows patients and their families to actively participate on the field and share their experience with cystinosis via the completion of an expert-developed medical questionnaire. The online registry was specifically designed to allow access from the privacy of one's home. Participants can rest assured knowing that their personal information is protected by three layers of security and that their answers are anonymous to anyone not directly involved with managing the registry.

To continue with the baseball analogy, once the ball players are assembled on the field, other people, such as spectators, reporters and scouts, with an interest in the game will be attracted.

With regards to the registry, interested parties could include researchers looking for data that will support their study proposals and help secure funding; clinicians who wish to increase their knowledge of cystinosis and better treat their patients; pharmaceutical companies that deal with orphan diseases and need to present information about the disease to oversight and regulatory bodies such as an Institutional Review Board (IRB) and the U.S. Federal Drug Administration; or investors who are considering investing in biomedical and pharmaceutical research.

Of course, another major and obvious benefit of this assembly of registrants is that clinical trial recruitment is made simpler and faster.

In essence, CCIR could serve as a convenient crossroads for all vested stakeholders where the setting for future cystinosis research is changed forever, and where the chances of "hitting a ball out of the park" and finding a cure for cystinosis are greatly improved.

Register at www.cystinosisregistry.org

Continued on next page

CCIR: BUILD IT AND THEY WILL COME *Continued from previous page*

ASK AN EXPERT

What are the current treatment guidelines for cystinosis patients that will promote the best health outcome possible?

1. Replace the numerous solutes lost in your child's urine because of damage to the kidney tubules.
2. Initiate cysteamine therapy as soon as possible and take as directed to reduce the harmful accumulation of cystine in the body's tissues.
3. Have cystine levels analyzed, preferably every six months, to ensure that cysteamine is adequately dosed.
4. Attempt to coordinate a 'team approach' to monitor your (your child's) health so that lines of communication are clear. Solicit input both from your primary care physician (your child's pediatrician) for day-to-day issues and a university-based nephrology or genetic specialist who can oversee the long-term strategy.

When do most patients start the use of growth hormones?

Growth hormone therapy requires daily injections and careful monitoring (additional blood testing and X-rays). It is also expensive, and not without the risk of complications. Consequently, it should be reserved for children who fail to grow when all other issues have been addressed. Correction of rickets is important for improving height, but there are a number of other problems that interfere with growth in cystinotic children. Nutrition should be optimized – this often means consultation with a nutritionist who is aware of the ongoing loss of sugar, amino acids and protein in cystinosis and, probably, caloric supplementation. Salt balance is crucial – the combination of indomethacin and oral salt supplements is often needed. Of course, acidosis should be fully corrected and cysteamine therapy should be optimized. When all these aspects have been dealt with (and given a chance to work), then growth hormone may be worth considering.

When is cysteamine eyedrop therapy necessary?

Cysteamine eyedrop therapy is recommended when, upon examination by an ophthalmologist, crystals are detected in the affected person's eyes AND the person has clinical manifestations such as photophobia (sensitivity to light) and/or eye irritation.

TODAY'S REALITY

It has been almost a year and half since CCIR was built and registrants have come from all ends of the earth.

CCIR is now 326 registrants strong, with representation in 32 countries.

Altogether, 16 sponsors and advocates from around the world stand behind the registry.

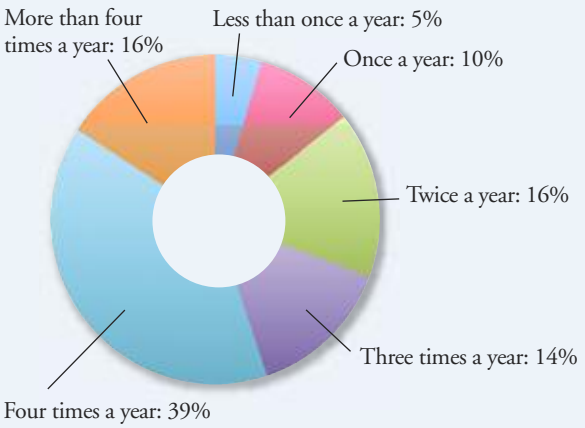
Forty-three registered professionals from 14 countries have come to the registry looking for information about the quality-of-life of cystinosis patients.

CCIR data has been cited in a 2012 academic journal publication by Stephanie Cherqui, PhD from The Scripps Research Institute, and at least one IRB application that we know of.

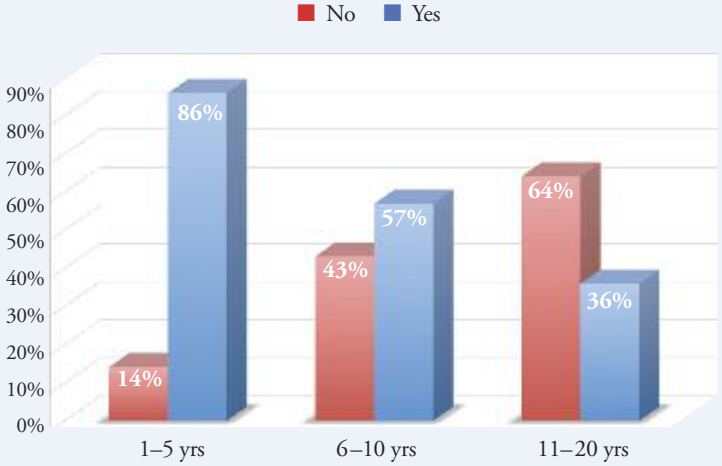
Awareness of the registry is gaining as CCIR presentations are made at conferences in the United States, France and Brazil.

In March of this year, a presentation about CCIR was made to cystinosis experts at the CRF Third International Cystinosis Research Symposium in Irvine, California.

Frequency of Regular WBC Cystine Level Testing (n=196)



Growth Hormone Use Among Registrants Ages 1-20 Years (n=193)

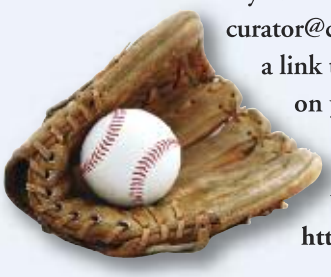


Perhaps equally exciting as the registry's success as a resource for medical advancements is it's value to patients as a trusted resource for expert medical information.

CCIR has received 46 questions from registrants through the *Ask an Expert* feature, available exclusively to enrollees. The questions range in content and cover topics such as medications, genetic testing and fertility. Medical experts in cystinosis who make up the CCIR Advisory Committee's Clinician Panel have provided responses to 100 percent of the inquiries received thus far. Periodically, the CCIR website FAQ page is updated with recent Question and Answer strings that have been de-identified (made anonymous) so that all registrants can benefit from the information.

We thank those who have contributed to CCIR's success thus far. It is still a work in progress, however, and there are still many who have not made it to "the field" and told their stories.

Please spread the word about how the registry is making a difference and encourage people to register. Also, help us keep the information in the registry current and accurate by updating your profile yearly.



If you have any questions contact me directly at curator@cystinosisregistry.org. Also, feel free to post a link to CCIR (http://cystinosisregistry.org) on your Facebook page.

Visit the CCIR website http://cystinosisregistry.org

CCIR PARTNERS AND ADVOCATES

CYSTINOSIS RESEARCH FOUNDATION

HELP US GROW BEYOND BORDERS
THE CYSTINOSIS FOUNDATION

Forever Growing
CYSTINOSIS FOUNDATION UK

Cystinosis Support Group
South Africa

cystinosis foundation ireland

Australian CYSTINOSIS Support Group

The Cystinosis Foundation
Cystinosis Foundation New Jersey Chapter
Cystinose France

Leben eben!

Tina's Hope for a Cure

Cystinosis AWARENESS & RESEARCH EFFORT

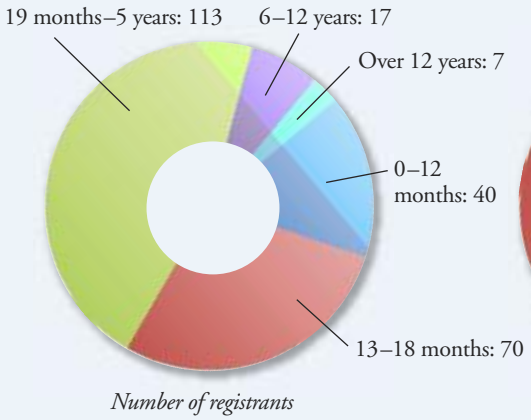
Jenna & Patrick's FOUNDATION OF HOPE

Joshua's Journey of Hope

HOPE FOR HOLT
REACHING FOR A CURE

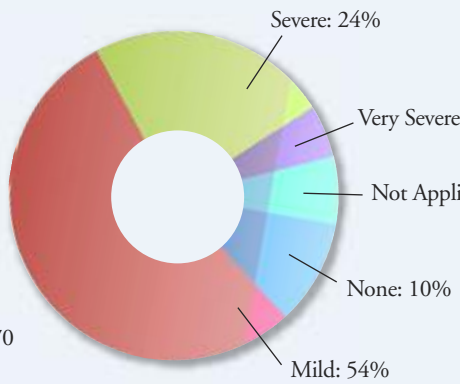
24 hours for Hank

Age Ranges at Which Eye Cystine Crystals Observed (n=247)

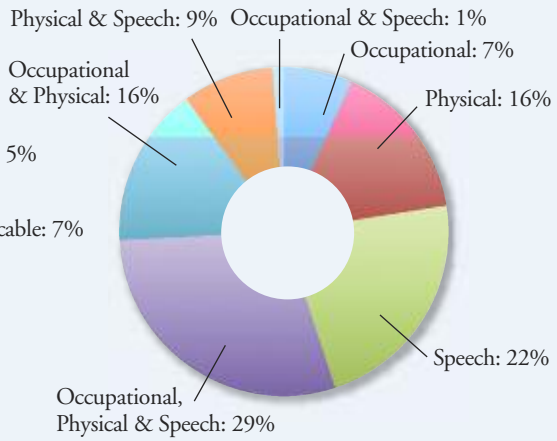


Number of registrants

Photophobia* Rating (n=269) (*Sensitivity to Light)



Physical, Occupational and/or Speech Therapy Used (n=89)

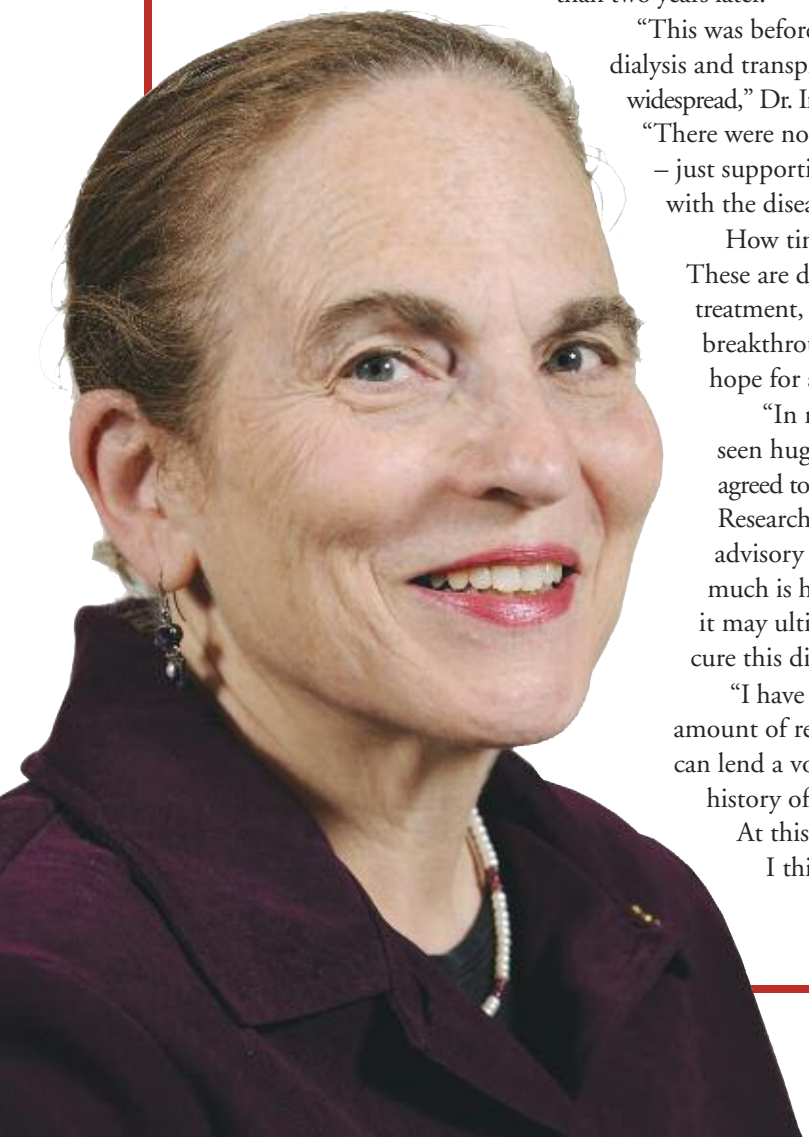


TAPPING FOUR DECADES OF EXPERIENCE, DR. JULIE INGELFINGER HELPS DRIVE THIS MOST DYNAMIC PERIOD OF CYSTINOSIS RESEARCH.

History in the Making

By Dennis Arp

It was more than 40 years ago, but Julie Ingelfinger, MD, remembers her introduction to the diabolic nature of cystinosis as if it were yesterday. For her, and for everyone else involved in the fight, those were the bad old days.



She was doing her training in nephrology, diagnosing and treating ailments of the kidney, and one of her most challenging cases was a 9-year-old boy with cystinosis. There was little Dr. Ingelfinger or her colleagues could do to help. The child died less than two years later.

"This was before cysteamine, and dialysis and transplants were still not widespread," Dr. Ingelfinger recalled. "There were no definitive treatments – just supportive care. Children with the disease did quite poorly."

How times have changed. These are days of life-sustaining treatment, of research-based breakthroughs and of genuine hope for a cure.

"In my lifetime, I have seen huge progress," she said. "I agreed to serve on the Cystinosis Research Foundation (CRF) advisory board because so much is happening, and, in fact, it may ultimately be possible to cure this disease.

"I have been involved in a fair amount of research and perhaps can lend a voice that knows the history of the field over time. At this point in my career, I think I'm in a good position to evaluate grant applications and progress, and I'm eager to make a difference."

Perhaps no one brings as much perspective to her role on the CRF Scientific Review Board (SRB) as does Dr. Ingelfinger.

In addition to being a senior consultant in pediatric nephrology at Massachusetts General Hospital, she is a professor of pediatrics at Harvard Medical School and deputy editor of The *New England Journal of Medicine*. In addition, on March 29–30 she co-chaired the Third CRF International Cystinosis Research Symposium at the Beckman Center in Orange County, Calif.

Dr. Ingelfinger is excited about the prospect of the delayed-release version of cysteamine gaining FDA approval, giving cystinosis patients and their families the chance to lead more normal lives. She's buoyed by advances such as cysteamine eye drops that combat the crystals that form in the corneas of patients.

She gains particular joy from the genetic research being done by Drs. Stephanie Cherqui, Corinne Antignac, Elena Levtchenko and others that "seeks to find ways to get affected cells to express the normal cystinosis gene and therefore be corrected."

"It's the possibility of an ultimate cure," Dr. Ingelfinger said. "I suppose the really amazing outcome would

be if one could correct the defect in the germ line, whereby someone with cystinosis not only would be cured but would subsequently be able to have children who don't carry the gene."

All of these areas of study are supported by the Cystinosis Research Foundation, as is a promising arm of research into genetic mechanisms that go beyond cystine accumulation.

But even as she ponders the possibilities for cystinosis patients and their families, Dr. Ingelfinger knows there is much work still to be done. Nothing would be more disappointing than to make decades of progress only to fall short when opportunities are within reach.

So she and her colleagues on the Scientific Review Board continue their collaboration to ensure that no area of research with potential for a breakthrough is languishing due to a lack of financial support.

The SRB meets twice a year to consider applications for funding from research organizations that have answered the CRF's call for proposals. The funding requests come from all over the world, representing both established organizations and others looking for a leg up on a new branch of research.

"One of the most exciting things about being a funding body for a foundation like the CRF is that we can fund startups looking to explore novel paths of research and treatment," Dr. Ingelfinger said. "It's not pie in the sky but something that seems feasible and just needs pilot data."

"With some of the larger, more general organizations, funding these types of programs just wouldn't be possible."

Also, by supporting fledgling organizations with a healthy number of its grants, the CRF has attracted a cohort of bright young researchers to the cystinosis field, she said.

"These are young people who will be major researchers in this area," Dr. Ingelfinger added.

Twice a year, members of the SRB receive a packet of proposals to evaluate. Dr. Ingelfinger's No. 1 consideration? "Will the project facilitate discovery with the potential to leapfrog existing research?"

Second on her list: "Will the effort draw in new investigators whose energy and expertise will benefit the overall cause of cystinosis research?"

Each proposal is considered on its own merits, and each board member brings a depth of knowledge that informs his or her critique, Dr. Ingelfinger said.

After many hours of personal consideration by each board member, the group engages in a vibrant discussion via conference call, the doctor said. "There's some give and take," she noted, "but we usually reach a consensus."

About 60 percent of proposals receive funding, and those that don't are often given notes so the applicants can improve and resubmit.

For Dr. Ingelfinger, the rewards of CRF service include seeing the cystinosis fight attract gifted researchers new to the field such as Dr. Robert Mak at University of California, San Diego, who is trying to better understand the mechanism of growth retardation and general muscle wasting in some cystinosis patients, and Dr. Allison Eddy of Seattle Children's Research Institute, who is investigating kidney scarring, among other research topics.

Dr. Ingelfinger will enjoy following their progress, as she has that of investigators who have previously received CRF support and who have helped fuel major leaps forward for cystinosis patients.

"One of the most exciting things about being a funding body for a foundation like the CRF is that we can fund startups looking to explore novel paths of research and treatment," Dr. Ingelfinger said. "It's not pie in the sky but something that seems feasible and just needs pilot data."

Considering Dr. Ingelfinger's career-long view to the grand arc of cystinosis treatment, it's telling to hear her call this the most dynamic and promising period in the history of the disease.

"From my viewpoint," she said, "it's very exciting to be part of an effort that is having such a positive effect."

THE YEAR'S MOST MAGICAL EVENING

Nancy and Jeff Stack
& Alex and Natalie

INVITE YOU TO JOIN THEM FOR

TEN YEARS OF

Wishes, Heroes and Miracles

2012 NATALIE'S WISH CELEBRATION

Honoring The Children And Adults Who Are Affected By Cystinosis

And Featuring A Performance By *On Broadway*

Saturday, April 21, 2012

6 pm Cocktails | 7:15 pm Program and Dinner

Balboa Bay Club and Resort

1221 West Coast Highway, Newport Beach, California 92663

For sponsorship opportunities or tickets,

contact Zoe Solsby at 949.223.7610 or zsolsby@cystinosisresearch.org

In a world filled with choices

thank you for making one that is having an immediate and lasting impact.

Whether you have attended an awards dinner in Sacramento, a soup and crackers sale in Ontario, Canada, a stein and dine in Lewiston, hit the slopes for a 24-hour ski-a-thon in Sandpoint, played golf in Santa Ana, or bought a lemonade or dressed to the nines for a gala in Charlotte you have helped the Cystinosis Research Foundation improve the quality of life for a group of children and young adults with cystinosis.

Many people have responded to the call for help. Their efforts offer new proof of the old adage that "many hands make light work."

Fundraising events have taken the shape of large-scale, high-profile celebrations and parties, as well as small personal efforts. They are being led by families and friends – by children, young adults and seniors.

Events are taking place in large urban areas and in small communities across the country – anywhere that people have heard about Natalie's wish, "to have my disease go away forever." Of course, Natalie's wish has now become the rallying cry for all those with cystinosis worldwide.

In 2011, the generosity of thousands of donors, large and small, totaled more than $2.6 million.

That extraordinary outpouring of kindness is making it possible for CRF to fund highly focused research at universities and medical centers throughout the world. That research is helping those with cystinosis today, giving them renewed energy and strength – and hope for a future free from cystinosis.

Jenna & Patrick's Foundation of Hope

Jenna & Patrick Partington
$325,725

Hope for Holt
Reaching For A Cure

Holt Grier
$151,161

Tina's Hope for a Cure

Tina Flerchinger
$112,440

24 hours for Hank

Henry Sturgis
$80,680

Cystinosis Awareness & Research Effort

Gabbie Strauss
$66,000

Joshua's Journey of Hope

Joshua Clarke
$20,050

Oliver Britten – *Letter Writing Campaign* – $37,335
Nicole Hall – *Running for Nicole* – $20, 357
Camden Sanders – *Help Camden Find a Cure* – $9,850
Landon Hartz – *Love for Landon* – $7,480
Addison Cox – *Addison's Angels* – $1,591
Bailey DeDio – *Bailey Believes* – $1,115
Whitney Glaize – $1,055
Glenn Jones – $1,010
Mary Head – $550
Eric Pekli – $425

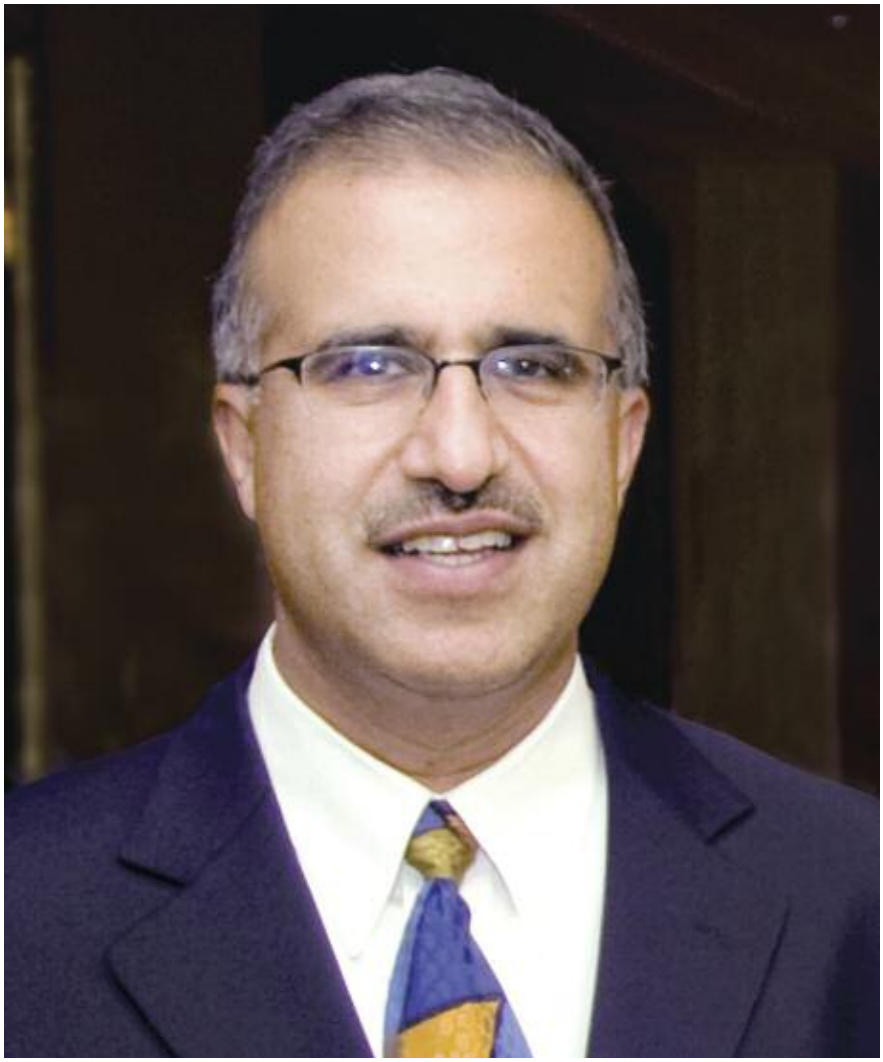
Totals for year ending 12/31/11

We genuinely appreciate your continuing support.

After spearheading a 12-year journey full of tests and triumphs, Dr. Ranjan Dohil is eager to see RP103 fulfill its promise.

THE PATH TO APPROVAL

By Dennis Arp



It all started with a simple question: "Why do these kids all have so many gastrointestinal symptoms?" Now, 12 years later, Dr. Ranjan Dohil has an answer that goes far beyond his original query.

Did we say answer? For cystinosis patients, it's closer to a godsend.

Soon Dr. Dohil hopes to see the research his question sparked reach its apex with FDA approval of RP103, the delayed-release version of the medication cysteamine. It's a breakthrough that heralds a huge improvement in quality of life for those with cystinosis.

To have this milestone moment within reach for patients means the world to Dr. Dohil, professor of pediatrics at UC San Diego (UCSD) Medical Center/Children's Hospital and Health Center. However, to jump straight from the project's inception to the promise of its culmination doesn't do justice to the journey.

The story of how RP103 sprang from an elemental question to become a profound opportunity underscores the depth of the commitment within the cystinosis community – a commitment to improve the lives of those most closely affected by this metabolic disorder.

Along the path of research and development, there have been some significant leaps forward, along with more than a few twists and turns, and even some dumb luck. But mostly there has been steady, heartening progress in the labs, the doctors' offices and the homes of patient families that together form the front lines of the cystinosis fight.

To reach a moment as significant as approval of RP103 takes more than an enduring commitment by researchers, Dr. Dohil noted. It takes strong partners such as the Cystinosis Research Foundation (CRF), which has provided the funds for research when no other source of support was available. And then there's Raptor Pharmaceuticals Corp., which has conducted the RP103 trials and stands ready to mass-produce the medication to help transform the lives of cystinosis patients.

When Dr. Dohil and his colleagues first decided to seek an answer to their gastrointestinal question, they had no idea how far the pursuit would take them.

"There was so much we didn't know about cysteamine, so even if our results weren't positive we knew that we could improve our level of knowledge," Dr. Dohil said. "But it turned out that the research was fruitful."

The inquiry began after cystinosis research pioneer Dr. Jerry Schneider called Dr. Dohil to enlist him in the search for the root cause of GI symptoms related to the disorder. The doctors and their colleagues were able to show that some acid production caused by cysteamine – the source of much of the nausea,

vomiting and stomach pain experienced by cystinosis patients – could be controlled with therapy.

As they progressed, "we started thinking about ways to improve absorption (of the medication), and to streamline uptake of cysteamine into the body," Dr. Dohil said.

Luck helped steer the team in the right direction. During the first study the team performed, looking at the production of stomach acid, a 4-year-old patient was supposed to be dosed via the stomach. By mistake, she was given cysteamine in her jejunum – the middle section of her small intestine. The next day she received her dose in the stomach as planned, and when results from the two days were compared, doctors found that the girl's gastrin levels were three times higher when she was dosed in the jejunum. That suggested the medication was much better absorbed via the small intestine.

"Basically that mistake in dosing is what triggered our thoughts on absorption," Dr. Dohil said. "With studies like these, it's always good to have a little luck on your side."

With that, the research team was off and running, with CRF funding allowing them to build momentum. The team's research, performed at UCSD, started revealing clues to cysteamine's pharmacokinetics – the mechanisms of its absorption and distribution throughout the body.

Dr. Dohil was ready to try what hadn't been tried before. He devised a tube about 16 feet long and had it custom-made in Australia, with a radio marker at the tip of a balloon on the end, "so we could always know where we were," the doctor said.

The tube allowed researchers to administer cysteamine in three areas of the body: the stomach, the colon (large intestine) and small intestine. By monitoring white blood cell cystine levels, they could determine which absorption site allowed the drug to be most effective.

"The results suggested that if we could target release of the drug in the small intestine, we could change the formulation and possibly get a drug that would work much longer, so it could be taken every 12 hours instead of every six," Dr. Dohil said.

Bypassing the stomach also reduced GI symptoms. The study's promising results were published in 2006, generating excitement in the cystinosis community. But the progress wouldn't have been possible without the courage of the early research participants, the doctor noted.

"Those kids were tough. Having a five-meter tube down your nose for seven days was no fun," Dr. Dohil said.

For the proof-of-concept study about 150,000 regular Cystagon® capsules were coated to delay release and target the small intestine. The study was supposed to last a month, but the results were so good that a number of the patients wanted to continue, and so the study was extended. Several of them are still on the medication six years later, which speaks volumes about the study's success.

In 2007, Raptor Pharmaceuticals joined the effort, producing the medication on a larger scale, spearheading studies that have moved things toward what is hoped will be FDA approval.

If and when that final hurdle is cleared, it will provide the ripest reward Dr. Dohil and his colleagues could have hoped for. Developing a delayed-release version of cysteamine, has given patients and their families the promise of more normal lives. Instead of taking medication four times a day, participants in RP103 trials have been on twice-a-day schedules, allowing them to sleep through the night, avoid so many GI symptoms and stay more compliant.

"For patients, it's massive," said Dr. Dohil, who in addition to his research and teaching regularly sees cystinosis patients. "To have to take medication four times a day every day of your life, affects your sleep rhythms and the lives of everyone in the family. It's the major reason kids become noncompliant with their therapy, which starts them down the slippery road to end-stage kidney disease and transplantation."

The delayed-release medication is not a perfect solution for cystinosis patients, Dr. Dohil said, but it is "incredibly significant."

Corinne Antignac, MD, PhD; Ted Daley, president of Raptor Pharmaceuticals; Stephanie Cherqui, PhD; and Ranjan Dohil, MD at the 2011 Natalie's Wish event, where they were honored for their longtime efforts on behalf of the cystinosis community.

Of course, Dr. Dohil isn't celebrating yet, because the finish line still hasn't been reached. However, he allowed, there are moments when he reflects on the 12-year journey and takes pride in how far he and his colleagues have come.

"I don't think about it a lot, but sometimes I step back," he said. "Let's just say that I'm happy with the way things have gone."

RP103 Enters New Phase of Journey

The prospect of RP103 gaining FDA approval has everyone in the cystinosis community excited, including the people at Raptor Pharmaceuticals Corp., which has committed its resources to developing RP103, or DR Cysteamine. As this form of cysteamine bitartrate continues to move through a safety extension study after successfully completing its pivotal, Phase 3 clinical study last year, and it is hoped toward global commercial availability, we wanted to catch up on its progress. Raptor Vice President of Commercial Operations Patrick Reichenberger provides an update, as well as a look at Raptor's plans for RP103's immediate future.

Patrick Reichenberger
VP of Commercial Operations
Raptor Pharmaceuticals Corp.

Q *What is the status of RP103 as we talk in mid-February 2012?*

A We expect to file with the FDA and the EMA (European Medicines Agency) in March, and we hope for a speedy review and approval process. The trials are done, but there is a standard safety extension study continuing. We have expanded the extension enrollment to include patients with transplants and those younger than six. We fully expect the drug to be used by these patients, just as is Cystagon®.

Q *How long might the approval process take?*

A Standard review would be 10 to 12 months. If we get accelerated review, it could be six months, which would mean we could have approval as soon as September or October.

Q *What is Raptor doing in addition to preparing the application and monitoring the approval process?*

A There is a lot of interest in this potential next-generation therapy, and we are making plans to help patients convert to RP103 as soon as possible upon approval. We are setting up a process to streamline the method of obtaining insurance approval for the drug. We will also be establishing patient assistance programs to ensure that everyone will have access to the drug, even if they have to go outside the normal insurance route. For patients, it will be good to schedule appointments with their physician as close to the approval date as possible. We will be sending out communications ahead of that date to keep everyone informed.

Q *Beyond distribution and patient communication, what role will Raptor play in the future of RP103?*

A Raptor looks to invest back into the community in terms of programs and materials and to partner with patients, caregivers and healthcare professionals to improve the overall quality of life for all those affected by cystinosis.

For example, we can help patients interact not just with their cystinosis physician but with their primary care physician as well. We can provide materials so primary care physicians can get a sense of what their cystinosis patients are going through and what their needs are.

Prior to launch, we'd like to get feedback from patients about how Raptor can best support them. We have already been doing that, but now we want to do it more formally. Raptor can provide a lot of value to the community, besides just RP103.

Raptor is also studying RP103 or other formulations of cysteamine bitartrate as treatments for other life-threatening diseases including Huntington's disease and non-alcoholic steatohepatitis. It's too early to say whether it will prove to be useful in those areas, but we are excited about the potential benefits of this drug for additional patients.

Q *Participating patients and their families obviously have played a role in the successful trials of RP103. In what other ways have you tried to involve members of the cystinosis community?*

A We've tried to get patients involved in any way we can. For instance, we hired one patient, an artist who lives in Europe, to provide input on the brand logo. One of the filters we're looking through on this drug involves the cystinosis community at large, so it's not the drug company on one side of the fence and patients on the other. We have relationships with our patients. Many of them have my cell phone number. Personally, I feel like I'm working for my friends. And when I see a patient with a needed skill, I see no reason not to bring that patient into the fold.

Q *What does it mean to you and to Raptor to have helped develop this delayed-release medication, which holds so much promise for those affected by cystinosis?*

A For any of us who have children, there is a particularly profound emotional connection to this work. I can't tell you how many times I've sat at a desk with tears in my eyes when I hear or read stories, especially from the clinical studies, about how lives have been changed for the better. It's hugely satisfying to be part of a team that's moving toward a common goal like this. What's the saying, "If you love what you do you'll never work another day in your life?" I think I'm pretty close to that.

Abbi turns six this year, loves animals and playing dress-up. She has a passion for fashion. Her favorite colors are pink and purple. Abbi is also an excellent big sister to three-year-old William. She has a cat named Cosmo, enjoys dance class, playing at the park, swimming in summer and making snowmen and snow angels in winter. She is crazy about crafts, coloring and making forts in the basement and backyard.

She is a beautiful girl inside and out. You would never know by looking at her that her body is in a battle every minute of every day. Many would never know that Abbi has cystinosis and most haven't a clue what it is.

Abigail Mary Monaghan BEAUTIFUL INSIDE AND OUT

By Katie Monaghan, Abigail's mom, St. Catharines, Ontario, Canada

To us, there are constant reminders that Abbi is unwell. However, we never use the word sick with her. Instead we explain that everything we do is to keep her healthy… eye drops every hour to reduce photosensitivity and prevent vision loss, (she also has a collection of cute sunglasses to protect her eyes and look cool,) life-saving medications every six hours. (She's feisty and determined, which just adds to the drama and excitement of administering such frequent doses!)

It's a full-time job keeping things "normal" in our world. Abbi attends a private tutoring program to help with learning difficulties associated with her condition and to allow her to keep up with peers at her "regular" school. She exercises to maintain muscle strength and attends ballet classes.

We try to maintain a balance of optimum good health by limiting contact with outside "germy" environments as much as possible without living in a bubble. Everyone who cares for Abbi makes sure the 2–3 liters of water a day she needs to stay hydrated is always near.

As an active young family we make sure she is getting enough rest because she tires easily. She tolerates smaller frequent meals and we feed her higher calorie food to maintain her growth and prevent the need for tube feedings. Getting up with her nightly as she goes to the bathroom, frequently needs soothing for a sore tummy, headache or achy legs is part of the ritual.

Our household budget is stretched to accommodate the extras that are important for Abbi's well-being. Insurance plans regard vitamin supplements as unnecessary. And extra costs at the grocery store to find the variety of foods that may tempt Abbi's poor appetite and monthly drives 1.5 hours each way to children's hospital for doctors' visits, eye drops, blood work and medications are not covered by insurance.

Abbi has many dreams for the future. She talks about wanting to be a teacher, a veterinarian or a children's doctor. Someday she would like to marry a boy she likes and be a mommy.

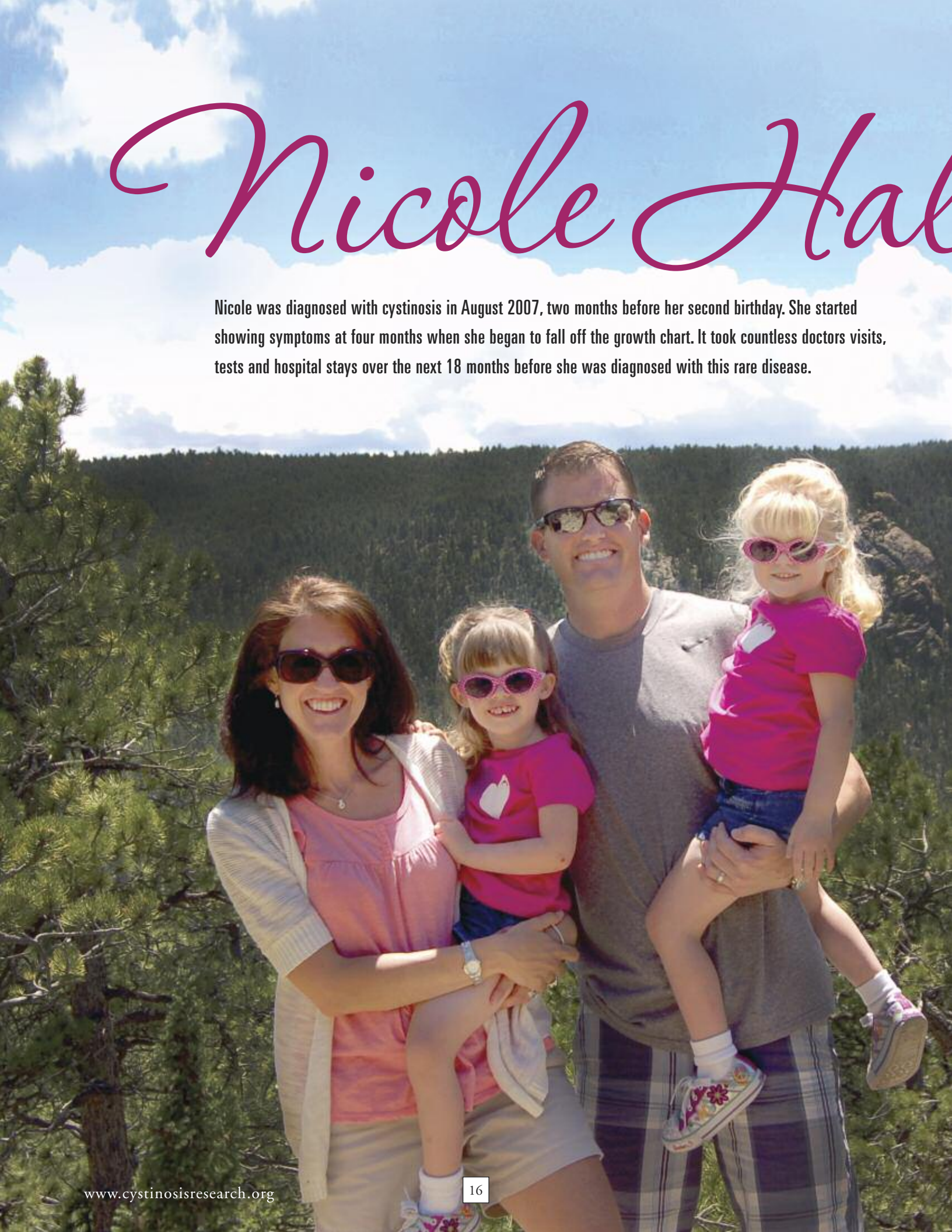
Growing up my parents taught me that with hard work I could be anything I wanted. They urged me to stand on my own two feet. They inspired me to do my best and encouraged me to be an independent person. We want the same for Abbi. Ongoing cystinosis research excites us. There is much that Abbi will be able to accomplish.

Even so, every night I go to bed and wonder… Will she have great friends to support her as we have? Will she find that special someone who accepts her for her? Will she experience the joy of raising a family? Will Abbi live to be my age?

Cystinosis has given our family a new way to look at life. However, we are ready for a cure…a cure so we can move on with our lives, be excited for the future and not fear the unknown.

Nicole Hal

Nicole was diagnosed with cystinosis in August 2007, two months before her second birthday. She started showing symptoms at four months when she began to fall off the growth chart. It took countless doctors visits, tests and hospital stays over the next 18 months before she was diagnosed with this rare disease.



by Stephanie Hall, Nicole's mom
Richardson, Texas

Nicole turned six this past October and is now in kindergarten. She has really taken to school and it is amazing to see how much she is learning. Whether she is reading, writing, doing math, speaking Spanish or learning about God, she is always willing to teach you what she learned that day. Her thirst for knowledge does not stop at school – for her birthday last year she asked for a telescope so she could learn about the stars and solar system. She is always excited when there is a clear night so we can set up the telescope and look at the night sky!

Stephanie, Angie, Aaron and Nicole Hall

The 4th annual Race for Nicole event was held in early December 2011 in Dallas, TX. We had three teams run the marathon relay at the White Rock Marathon. In 2012 we plan to expand beyond running just the marathon – Race for Nicole will host our own 5K races in both Dallas and Denver.

Nicole's school has been very accommodating and has adjusted well to her schedule. The school nurses are happy to administer her daytime feeding, which she receives through her G-tube, and her midday cocktail of medications and eye drops.

Her classmates recognize that she is different, but they deeply care for her and surround her with love. It is not surprising that Nicole wants to go to school every day, even when she isn't feeling well.

In February of last year we had a bit of a scare when she got sick and spent six days in the pediatric intensive care unit. It was a painful reminder that children suffering from cystinosis have such fragile systems, how important each medication is, and how a small adjustment can have serious impacts. Thankfully, she came out of the experience a healthier and happier kid.

Nicole has started to understand that she is "special" and we know that one day soon she will start asking the difficult questions about her disease – we only hope that the research funded by the CRF community will help make those questions easier to answer when that day comes.

We are deeply grateful for everyone who donates their time, effort and financial support to finding a cure for cystinosis. It is this support that gives us hope for Nicole and the other children suffering from this disease.

Amid the Trials,

Addison Cox
Wake Forest, North Carolina

Photo by Lars Wanberg

By Dennis Arp

Anyone with a child who suffers from a serious ailment knows it's not always easy to provide a fresh answer to the questions of well-meaning friends. Nicole Cox knows, because people are always asking, "How is Addison doing?"

She goes straight to the truth.

"It's funny, but I tell people we're either really good or really bad – it doesn't seem like there's any in-between," Nicole said of her daughter, who was diagnosed with cystinosis at 18 months and is now 3½.

"These days Addison is in the 25th percentile for height and weight. There was a time when I never thought we'd get up to that mark. So now I say, 'I don't care if she is little, at least she's on the chart.'"

Celebrating the small victories is one of the lessons Nicole and her husband, Brandon, have learned from dealing with Addison's illness. Another is that there are no small victories; every triumph is big when your daughter has cystinosis.

Sometimes just getting through the day is victory enough for Nicole. In addition to Addison and her illness, Nicole also cares for Addison's sister Emma, who is 20 months old. And on March 12, she gave birth to their third child, Lily Grace.

"It's a difficult balancing act," Nicole said. "There's no way I could get through what we've been through without a very supportive husband and a family that helps. But it is hard.

"Sometimes I wonder why God thought we could handle all of this, because there definitely have been a lot of times when I felt we couldn't handle it."

Nicole has been facing the special challenges that go with caring for a newborn and having to administer a daunting and ever-changing array of medications to Addison. There is also the care and maintenance of Addison's gastric tube. And the seemingly constant cleaning up of vomit. And the perpetual changing of sheets either soiled or sweated out.

"It's a challenge physically and emotionally," Nicole said. "But then it was the same when Emma was born."

Nicole allowed that there are concerns for their new baby, given that cystinosis is a genetic disorder. However, those thoughts quickly transport her to the overriding reality of her life: that "Addison is the biggest blessing

We walked in (to the CRF Day of Hope Family Conference), and it was like we had an instant family. We were with people who knew exactly what we were going through, who could explain what was coming next and give us ideas on how to do things. It was a great experience.

NICOLE COX

Nicole Cox Finds Moments to Behold

for our family," she said.

"She teaches us every day about the most important things. Even though she's young and been through so much, she's so happy. She's amazing."

Nausea and vomiting are so common for Addison that sometimes she will throw up and in the next moment be smiling and laughing. Nicole said that she appreciates her daughter's resilience, but she can't help but feel a twinge of sadness.

"I hate that this is her normal," she said.

Nicole also appreciates the friendships she has made in the cystinosis community, especially since her husband travels a lot for his work. At least monthly she talks with members of a handful of families who share strategies on coping with the disease.

"I know that if I ever needed anything, they would be right there for me, as I would be for them," she said.

Nicole still has vivid memories of her acute need for information and support in the head-swimming days immediately after she and Brandon got the news that Addison had cystinosis. Their doctor told them not to search the Internet because they'd likely encounter a lot of misinformation that would only fan the flames of their fears. But he did suggest they search out the Cystinosis Research Foundation (CRF).

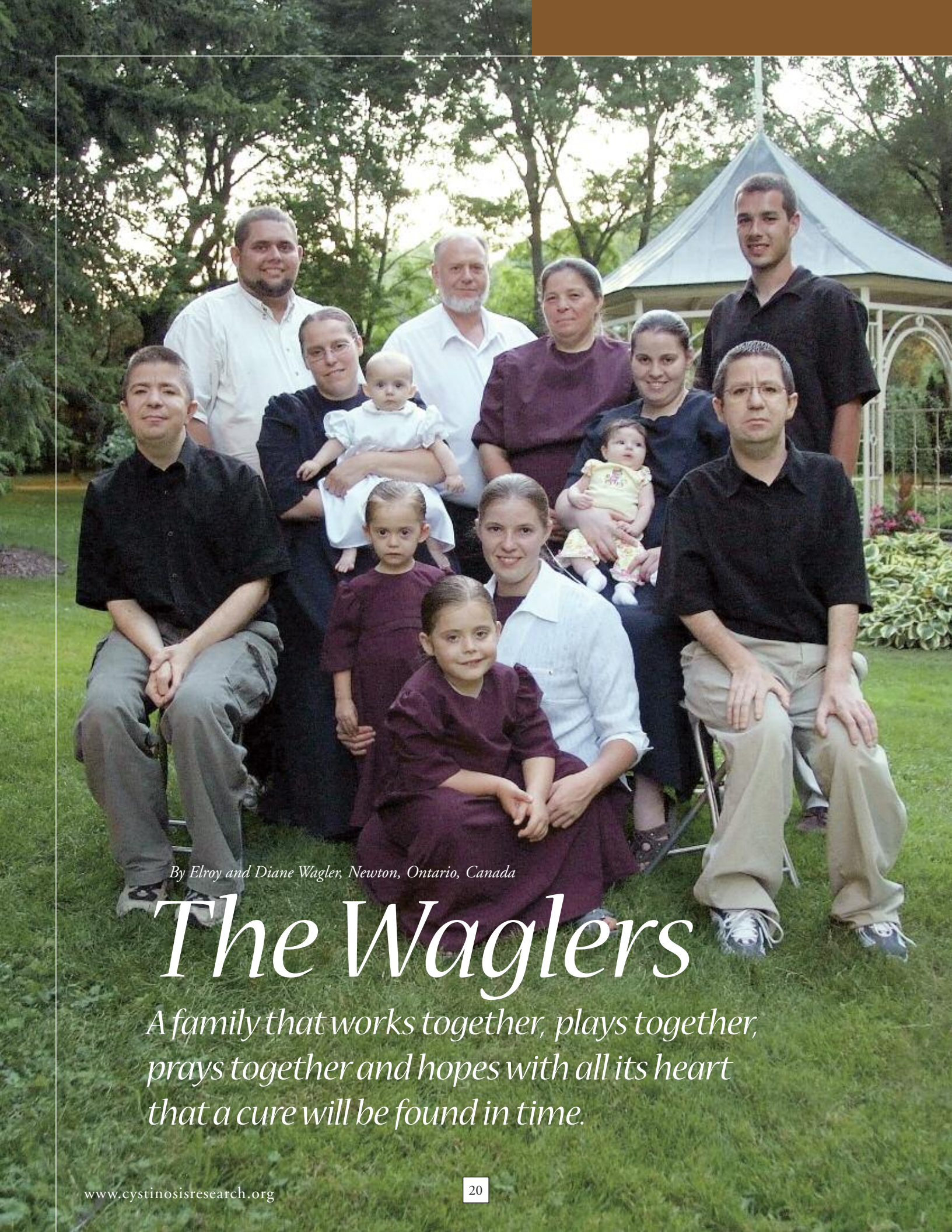
At the foundation's Web site, Nicole learned about the upcoming CRF *Day of Hope* Family Conference, and she knew she and her family had to be there.

"We walked in, and it was like we had an instant family," she said. "We were with people who knew exactly what we were going through, who could explain what was coming next and give us ideas on how to do things. It was a great experience."

Many trying experiences have followed, and many more are probably on the way. But Nicole and her growing family are finding the strength to endure the bad days and celebrate the moments when things go well.

"We're so much more hopeful than we were in the beginning," she said. "I can believe Addie will go to college and do lots of other things. That makes it easier to get through the days when things are rough."

Nicole Cox with her daughters Emma (left), Addison and new sister Lily Grace.



By Elroy and Diane Wagler, Newton, Ontario, Canada

The Waglers

A family that works together, plays together, prays together and hopes with all its heart that a cure will be found in time.

Our whole family –

Elroy and Diane Wagler, Timothy and Nathanial (both with cystinosis), Anita and Joseph Gerber, Lynette and Ryan Jantzi and Loretta – wants to thank everyone who has put so much effort into finding a cure for cystinosis even though the cure may be too late for our sons.

We know firsthand

about a parent's heartache when they learn their child has an incurable disease.

We know what it is like

to watch them as one part of their body after another is destroyed.

We know the hurt

that a parent feels when their child finally realizes they have a disease that will destroy them and take their life.

We don't want those

we love so much to go through such hard times.

Our first son, Nathanial was born July 22, 1980. He was a healthy strong baby who grew fast until he was four months old. After that, he did not gain weight. At six months he started to drink water and urinate excessively. He was always thirsty and his first word was "wa wa." I remember when Diane would turn on the tap in the kitchen and Nathanial would crawl across the floor and tug on her dress to get a drink of water. His appetite diminished and he would vomit what little he did eat. He slept very poorly and cried all day and night.

At nine months he was so sick he ended up in our local hospital. When they couldn't diagnose Nathanial locally, he was referred to a pediatrician in a larger city. At first the pediatrician thought Nathanial was stubborn and told us to take all water away from him. Finally, the pediatrician realized that something was seriously wrong and referred Nathanial to Sick Kids Hospital in Toronto, Ontario. On that day in May 1981 we left the doctor's office with heavy hearts and a feeling that this was something quite serious.

Even though we expected something serious, the words "incurable disease" hit hard. Parents who receive this type of diagnosis know what a crushing blow it is. We cried on the way home that day. It was hard to adjust to handling all the new medications and to managing the tiring trips and long days at the clinic. Nathanial's first hospital stay was very difficult. These are some of the memories I just wished I could erase.

Continued on next page

Nathanial Wagler

On August 5, 1981, three months after Nathanial was diagnosed with cystinosis, our second son Timothy was born. He was such a contented baby. During his first exam at five weeks, the doctor told us that he didn't have cystinosis but by 13 months he developed excessive thirst and urination. In September 1982, Timothy was diagnosed with cystinosis. It took all our courage to handle the news that our second child had cystinosis.

Our third child and first daughter, Anita, was born on December 9, 1982. We just watched and worried about her but thankfully, she was healthy. Today she is married and has four dear children.

Our house was busy with a new baby girl and the two toddlers with cystinosis. We did lots and lots of laundry because of the excessive urination and cloth diapers. It was very tough.

On July 31, 1986 our fourth child, Lynette, was born. Again, the doctors didn't test for cystinosis. Today she is married and has one lovely little girl.

When Nathanial was about 8 years old, his kidney started to fail. It was difficult to watch Nathanial and Tim go to school, knowing they felt so bad. Because of the cystine crystal buildup, their eyes became extremely light sensitive and they could barely see in the sunlight. In December 1988, Nathanial had one kidney removed and we began peritoneal dialysis.

On March 31, 1989 our fifth child, Loretta, was born. Within a few days our doctor happily told us that she was okay. Today she is a healthy 22-year-old.

The summer of 1989 was especially difficult. We had five young children, including two with cystinosis. Nathanial's condition was very unstable and we travelled four hours a day, four times a week to and from Toronto for dialysis. Despite our efforts, Nathanial was sinking fast. The situation was more than we could handle physically, mentally and financially. Our church stepped in and arranged to have someone take Diane and Timothy to the dialysis appointments. This was such a relief and a blessing.

On December 3, 1989 Nathanial had his transplant. Within a week he had a lot of energy and a good appetite, and so, within 14 days he was home.

Timothy began dialysis in spring of 1991. We did hemodialysis but it didn't work well for him so we switched to peritoneal dialysis. Because of all the complications, he was in the hospital from November through February. He received his transplant on December 14, 1991. Our youngest daughter was almost 2 years old at the time and we feel like we missed out on her baby days. We're still trying to make up for it.

The years from 1991–2004 flew by quickly. Life was somewhat normal. Our sons were blessed with two good transplants. When Nathanial and Timothy were teenagers we were introduced to Cystagon®. It was a difficult time to start taking the drug because of all the side effects. Cystagon® caused Nathanial so much abdominal pain that he stopped taking it. Tim took a higher dose of Cystagon®, but his cystine level always stayed high. Our boys could only tolerate Cystagon® for about 2 years. I'm afraid to say that I had very little faith in Cystagon®.

Nathanial has always had a big heart for others. Even as a youth, if he saw someone hurting he would take them out for a meal or somewhere fun. His big heart has touched many lives.

In 2004, Nathanial began having trouble swallowing and would choke while eating. I feared this had to do with muscle function. Our sons saw Dr. Howard, who was very caring. They were his first cystinosis patients. After 3 years of struggles the doctor recommended gj-tubes. It was a good way to care for the boys because they could take their meds and most of their fluid through the tubes.

Our challenges continue in 2012. Nathanial is now 32 and Tim is 31. Nathanial's strength is diminishing and Tim suffers from severe nausea.

Sometimes we have to accept the fact that we can't do it all. Wearing ourselves to a thin thread is not the answer. At times we have to humbly accept help graciously offered to us.

My family doctor recently told me that he doesn't know how we do it. I told him that the work of caring for Nathanial and Tim is easy, but the emotional strain and stress that goes with it cannot be put in words. We thank our Heavenly Father first for providing for our needs and also for the medical help we received. Without His help, we would not have had our dear sons for this long.

It is difficult to watch cystinosis take its toll on your children. You see potential and talent developing in them and at the same time you watch the disease progressing, taking their strength and health away to the point that their talents can no longer be utilized.

When Timothy was feeling good, he was very neat and artistic and he enjoyed landscaping and caring for our flower beds. He has a natural talent for drawing, painting and making business signs. He even painted the sign for own business, Colonial Brick and Stone Inc.

Continued on next page

Nathanial was close to animals and soon had our dogs jumping through hoops and did a very good job of training, riding and showing horses. Nathanial spent a lot of time working at our family business and became an excellent Production Facility Manager. As he grew weaker, he finally announced that he could no long continue in the position he had filled so well. It was a huge disappointment and we miss him so much.

Nathanial always had a big heart for others. Even as a youth, if he saw someone hurting he would take them out for a meal or somewhere fun. His big heart has touched many lives.

We always felt it was important to be honest with our boys about the seriousness of cystinosis. Nathanial says that even with his condition, he is going to enjoy life as long as he can.

Timothy is more of a worrier and developed depression. Our boys grew used to getting many blood tests and other painful tests. Timothy would hold out his own arm and when the nurse finished the blood draw he would thank her. We were so touched.

Sometimes we have to accept the fact that we can't do it all. Wearing ourselves to a thin thread is not the answer. At times we have to humbly accept help graciously offered to us. If not enough help is offered, we may even have to humble ourselves further by asking for it. However, no matter how much our friends do for us, the weight of it all is still there, which is hard on us and not always easy to cope with. Sometimes I am forced to remember that if our burden is hard to bear, what about those who have the disease?

I remember times when people cared enough to slip some cash into our pockets, or offered to drive us to the hospital or help with a fundraiser.

Our family has received many acts of love and kindness. We have to dwell on the good to remain strong.

Even when we are physically drained, as parents we have to be so careful and remember to reach out to each of our children so they don't feel left out. They have needs too.

A disease in the family takes its toll on everyone in the family. We need to be careful so we don't hurt the ones we are closest to and love the most. I hope we all make the wise choice. When we endeavour to encourage others, guess who gets the big blessing?

One couple commented to us, "God must have tremendous confidence in you to place two boys with such challenges into your care."

We keep our focus on the good things and times in our lives in order to keep our spirits up. We must do all we can to brighten the corner of world where we are.

Even though Diane and I have to be pillars of strength for our children, it's good for them to see that we still care enough to cry. The night Nathanial told me, "Dad, I kept eating for as long as I could," I just broke down and cried and cried.

When we were young and newly married Diane and I had hoped to go on a mission project somewhere. We soon realized that wouldn't work out and understood what our real mission was. We had two sons who needed special care, so we focused on being the parents they needed.

We keep our focus on the good things and times in our lives in order to keep our spirits up. We must do all we can to brighten the corner of the world where we are.

Although time is running out for Nathanial and Timothy, we still have hope. Our hope and prayer for everyone is that a cure can be found before the ones you love experience too many of the disheartening things that are a part of cystinosis.

WE ARE TOUCHED BY THE EFFORTS OF OTHERS TO FIND A CURE, AND WE WOULD LIKE TO DO WHAT WE CAN TO HELP.

The Wagler family business, Colonial Brick and Stone Inc., would like to donate a prebuilt, 72 foot, weather-edged Manitoulin Island limestone waterfall. This magnificent natural waterfall would be an asset to any business, golf course or personal estate.

If you know anyone who would be interested, please contact Elroy Wagler at 519-595-4261 or Trevor Strauss at 519-590-9495, trevors@cystinosis.ca.

Dancing in the Rain

By Amy Krahe, Jake's mom
Broadview Heights, Ohio

Nearly a year after Jake's diagnosis, I read the quote, "Life isn't about waiting for the storm to pass. It's about learning to dance in the rain." It moved me, and has since been adopted as our way of life.

Jake is five years old, and for the past year, he has been growing and doing very well. It has been a slow process, but he has made significant progress. Jake has a joyful, outgoing and adventurous spirit. He enjoys fishing, riding his bike and playing any and every sport! His most recent adventure is learning to snow ski. A few falls, a few laughs ... a few more falls and finally, he was ready to take on the ski lift! He is strong, resilient and embraces life with all his heart!

Lately, however, the course has changed. Jake has been telling us his eyes hurt. He doesn't understand why they hurt, but I know. It's proof. The darkness of this disease is slowly, but surely progressing. As we scheduled his first appointment at the National Institutes of Health a sadness fell heavy on my heart. After I pulled myself together, I looked for strength.

Strength comes in many ways. Our family and friends support and love us and with that alone we have strength. The cystinosis community offers hope, guidance and encouragement that words cannot begin to describe. But there are less obvious ways I find strength: the strength that comes in small doses, every day. Those simple and genuine, everyday moments that bring a smile to my face and freedom to my heart.

I love everyday moments. It always makes me smile when I give Jake his meds in the morning and he pretends he's sleeping, upside-down and smiling. Or when we play Candy Land, and he wraps his arms around my neck, wearing a huge smile and 'ba-a-a-lks' like a chicken. Or when I listen to him and his twin brother Austin put on a magic show for all their stuffed animals. These are the moments I enjoy most.

And, these are the moments that give me strength. Everyday moments that remind me to live a little more like Jake. To love and laugh without holding back. To embrace the joy of today and to always make time to dance in the rain. If ever I need strength, I always think of Jake ... upside-down and smiling.

Gabbie and Chloe at the 2011 CRF Day of Hope Conference

Photo by Lars Wanberg

By Jody Strauss, Gabbie's mom
Waterloo, Ontario, Canada

Gabbie Strauss
A VERY SPECIAL BIG SISTER

Our little Gabbie is now 4 years old and a junior kindergarten student. The transition to school went better than we expected. She loves school, her teacher and all the really cute kids in her class. We've been blessed to have a warm and caring secretary, Mrs. Geus, who gives Gabbie all of her medications and supplements. The school has done an amazing job of giving Gabbie everything she needs on time.

Gabbie often has long nights. She wakes up to drink water, up because she soaked her pajamas and sheets, woken at 1 a.m. for meds and awake again at 6 a.m. to eat breakfast before her morning meds. I sometimes wonder how she will get through the school day without collapsing. Trevor and I have espresso and coffee to keep us going, but water and apple juice doesn't seem like it will cut it after sleepless nights. I'm always amazed how she perseveres. She has made it through every day with a smile and she hasn't been sick once this school year.

To the outside world, we appear to be a normal, healthy family. Unfortunately, that couldn't be further from the truth. Normal for us means preparing 22 syringes a day, washing them, drying them, and worse, giving them to our 4-year-old. I find syringes all around our house, they take up way too much room on our counters and they are a constant reminder of Gabbie's condition.

Gabbie and her sister Chloe like playing with syringes. They play doctor and give their dolls "ouchies." Chloe likes to pretend that she takes supplements too. On the rare occasion when Chloe has to take Tylenol, she is so happy she gets to have a real syringe just like her older sister. Yes, our house is a little unusual. Normal for us also means waking up every night at 1 a.m., no matter how physically exhausted we are. Normal means washing wet sheets and

pajamas that are soaked with urine day after day. Normal means a state of panic if or when we leave our house without water. I remember one afternoon on the way to swimming lessons, Gabbie asked for water and we realized that her sippy cup was in the trunk. There I am at a stop light, hopping out of the car and retrieving the water before the light turns green. These are some of our not-so-normal life with cystinosis moments.

As Gabbie gets older, she is starting to tell us more about how she is feeling. Lately, she's been telling us that something is in her eyes and she is rubbing them more. I assume the cystine crystals are to blame. She has also told us that her supplements (as we call them) "taste yucky." As a parent, it is difficult to hear these things because there is nothing we can do to make it go away. I listen to her, love her and focus on our many blessings. I stay strong for Gabbie, but behind closed doors I allow myself to feel sad for a few moments.

> *"After I pray, I have a renewed sense of hope, faith and joy and I believe that better days are ahead. Something in my heart says that everything is going to be ok."*

On February 24, Dana Shortt Gourmet in Waterloo graciously hosted a *Winter Soup & Cracker Fundraiser* in support of cystinosis research. Once again, we were totally overwhelmed by the kindness of others. Our community has a big heart. Faithful friends and supporters from our church, school, neighbourhood and city came out on a snowy, blowy day to purchase soup to help our family.

The staff and teachers at Gabbie's school placed a huge order for soup and sent a notice to all the parents. Dana's delicious winter soup flew off the shelves and her chef had to quickly make more to meet the demand, but even that sold out. Lots of soup and lots of love for Gabbie made for a very successful event that we will never forget.

Gabbie and Chloe love to visit their 86-year-old great nanny, Phyllis Schriver

The Kente Kiwanis of Trenton 'stand behind' Gabbie at 22 months

One of Gabbie's biggest fans is Terry Broderick of the Trenton Kente Kiwanis Service Club from my hometown of Quinte West, Ontario. The Kente Kiwanis had the city of Quinte West declare an official *Gabbie's Wish Day* and they worked very hard to raise over $15,000 for CRF. The Kente Kiwanis continue to support us year after year. They have touched our lives and we appreciate their love and support so much.

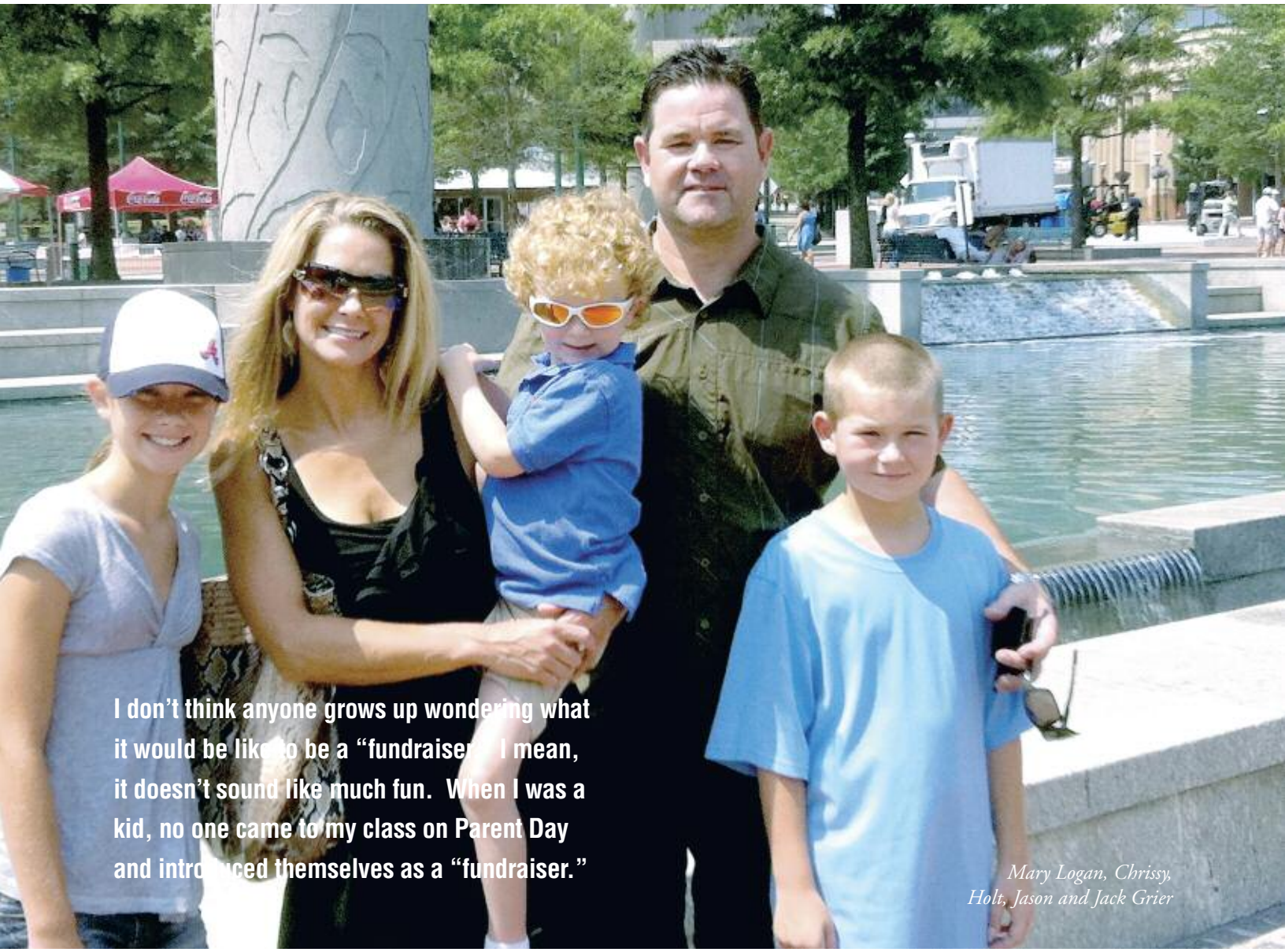
We are thankful for each new day and we find joy in unexpected places. Some people 'stop to smell the roses,' but Gabbie and Chloe prefer to 'stop and pick up sticks, stones, chunks of ice or snowballs' as we walk to school. I try not to rush them and I let them take a moment to enjoy the small, simple things. Cystinosis has taught us not to take a single day for granted.

I can't imagine our life without the hope of the Cystinosis Research Foundation. They give us a reason to keep believing, keep hoping and keep dreaming for the day when cystinosis is cured forever.

Hey Mister

"Wanna Buy a Rock?"

By Jason Grier, Holt's dad
Cornelius, North Carolina



I don't think anyone grows up wondering what it would be like to be a "fundraiser." I mean, it doesn't sound like much fun. When I was a kid, no one came to my class on Parent Day and introduced themselves as a "fundraiser."

Mary Logan, Chrissy, Holt, Jason and Jack Grier

My dad was a salesman, my mom a teacher. Other parents came to class and they were also salesmen – or engineers or mechanics or cooks. There was even a doctor and a lawyer. I didn't find any of it overly interesting but I always thought it was cool when a dad came and had his name on the front of his shirt. One kid down the hall had a dad who was a professional wrestler – I always wanted to be in that kid's class.

Me…I wanted to be an athlete, a lawyer AND a scientist. In my imagination, I would score lots of touchdowns, win every case with a last second "aha" just like Perry Mason, and make green bubbles and steam come out of a beaker like I saw them do on TV.

I had a great childhood. I lived in the same place all of my life, so over time I got to know lots of people through sports and school and had friends at different socio-economic levels. As I grew older I recall thinking that some of my friends lived in really big houses. I realized that when they invited me to the "club" to go swimming, there was also a golf course and tennis courts. I also realized that the people who were socializing at the club were all dressed really well.

As I grew even older and started reading the paper, I saw pictures of my friends' parents – the ones from the "club" – in the paper and they were always dressed to the nines. As I read about them, they were always doing something really nice for

someone else – usually donating lots of money to a particular cause. I remember hoping that one day I could be in the paper for giving money away, which would mean that I REALLY had a lot of it!

Like most people, I guess I assumed that raising money was something that rich people did, so I never really thought much about it. I was just out of college, barely making ends meet and trying to decide if I was going to have Pizza Hut or Dominoes for dinner. My focus was on doing my job, getting better at it, and figuring out how I was going to meet some very ambitious goals before the age of 35. It never dawned on me that having a cause and raising money for that cause would be something I would ever have to do.

Then came the news: My son is terminally ill. Not only is he really, really sick but the treatment regimen really stinks. Not only does the treatment regimen really stink but there isn't much information out there about the disease – and I have a lot of questions. What are we going to do?

The first thing I decided to do was learn all I could about the disease – where to go, what to do, who to ask for help, etc. I knew that it would take my wife and me some time but it would become our new "normal" – exhausting but normal. After that, I wanted to reach out to others who were in the same boat and learn from them. I instantly realized that there was a unique bond between us all. When I spoke to a parent of a child with cystinosis I always knew that we had a new family member I could – and still do – turn to.

From there, I had to figure out how to move forward.

The way I saw it, we had three options:

1. Lean on my family and try to live as normal a life as possible.
2. Learn more about the disease, the research and the long-term prognosis and stay informed about what was happening with those who were working on the science.
3. Go public within my circle of friends and community and do whatever we could to get the word out and/or raise whatever we could to help drive the research.

We initially chose to pursue options 1 and 2, but option 3 quickly and spontaneously occurred at an informal get-together of some high school buddies.

We were sitting at a table eating when one of my friends asked about Holt. I nervously told them about Holt's condition, his medications and the long-term prognosis. I lowered my head so I didn't get emotional as I talked. Then, someone else spoke up and said, "Let's do a golf tournament to raise money for cystinosis." Someone else added, "Let's throw a party" – another spoke up and then another. I just sat there in shock. I didn't really know what to say. It was so nice and thoughtful and selfless of them – I certainly couldn't say no.

That's how it all started. First, a neighborhood walk put on by the Doerings, who lived next to us. They recruited a few friends; we encouraged a few others to come; my family invited some of their friends and before we knew it – we had raised $11,000. My friend Tom Hughes flew down from New Jersey with his son and flew home that same day – and they have flown down every year since. Many of my childhood friends and neighborhood friends showed up. They didn't know much about what we were going through but when they heard about the disease and the work that the Cystinosis Research Foundation was doing, they wanted to know more.

As they learned more, people grew more emotionally invested because they believed they were truly making a difference. When you donate to CRF, you know that every dollar goes to research and that the research is actually making things happen. How many other nonprofits can boast CRF's success in such a short time? Not many, if any. It's a great story and everyone who hears about it wants to be a part of it.

From that neighborhood walk it began to grow. Some kids on the street had a lemonade stand and donated the

continued next page

proceeds to CRF. One kid sold me a rock he found in the mud for a buck and then donated the money to CRF (I gave him his rock back).

Momentum was growing and we were just getting started.

My childhood and high school friends and my very special sister-in-law, Aubrey decided to hold a gala. **A GALA?** I didn't even know what that meant but they rented a neat place in town – and I knew that I had to get dressed up. We invited everyone we could think of but we were still afraid that the event was going to be a bust.

Fortunately people came. My childhood friends were there and my Sigma Chi fraternity brothers came in droves (and still do). Friends of friends, and friends of family, and new friends we'd never even met came. They all showed up and we filled the place. But no one was sure how we should act. Should we be happy and celebrate because we were all together? Should we be sad because this cruel disease was doing terrible things to kids. Looking back, there was a lot of sadness and happiness in the room that night. In the end it was a great event – and we raised $75,000!

After the gala, another friend invited us to halftime at a football game to introduce us to the crowd – $2,500 raised. Girl's Night Out – several hundred dollars raised. The people who clean our home, and who we didn't actually know very well but who have HUGE hearts, wanted to do something – a golf tournament and a change drive – $16,000 raised. It kept going and going and going – events were popping up everywhere almost on their own.

People were learning more about CRF and they wanted to help. It got to the point where we literally couldn't keep up. Finally my family and my buddies got together and decided to help in a more organized way. We decided to form a charitable foundation and hold a formal event each year. And the rest is history.

What started as a conversation with some high school friends has grown into an organization that has donated nearly $1 million dollars to CRF since 2007.

Here is the point – you have to tell people your story. I'm no fundraiser or at least not a very good one and I'm scared to death to ask people for money. I am fortunate to have a wonderfully strong family, an incredibly driven sister-in-law and the best friends in the world. I'll bet they are a lot like your family and your friends. The more they heard about our story, the more they wanted to get involved. The more they got involved, the more others got involved. The more others got involved, the more people attended our event and learned that donating to our charity really makes a huge difference in people's lives.

I never played professional football or won a case with a Perry Mason "aha" moment. But what I do get to do is pretty cool – help to raise money for CRF. That money helps some talented and dedicated scientists discover better treatments and hopefully, a cure for cystinosis. Our collective efforts have changed my son's (and many others) life forever.

By the way, I was wrong about who gets their picture in the newspaper. You don't have to be rich – and you certainly don't have to be rich to make a huge difference in the lives of others. We have some very successful friends who give us a lot of money and we certainly appreciate them a lot. But we also have friends who give less money and we love them too. I mentioned the wonderful lady who helped maintain our house – she raised $11,000 not because she was rich – far from it. She did it because she was inspired and felt a calling to make a difference.

If you are reading this and have a child newly diagnosed with cystinosis and are wondering how you can help, here's my advice: take your time and get settled into your new "normal." Once you are there, you can pick from any or all of the three options I mentioned earlier. Then decide how you want to move forward.

If you have been in our community for a while and are wondering how you can start to raise money, here is my advice: find a positive person … someone who gives you energy … tell them your story. I guarantee you won't regret it.

Who knows – it might be a muddy rock that turns into a million bucks.

5th Annual Hearts for Holt

Hosted by Brandon and Aubrey Grier, the 5th annual Hearts for Holt event to benefit the Cystinosis Research Foundation was held on Saturday, February 4 at the Charlotte Country Club.

The event was another spectacular success for the Hope for Holt Foundation.

More than 250 people turned out for the gala event that raised nearly $200,000 for cystinosis research. Over 100 silent auction items and eight live auction items were sold that evening including a once-in-a-lifetime trip to Aspen, Colorado for one week at the Coldstream Trout Lodge.

With a professional auctioneer conducting the festivities, the room was in stitches as we played "heads or tails," "hi-lo" and "champagne pong" for cash prizes, an iPad2 and a beautiful necklace valued at over $1,000.

One Stop Live provided the entertainment for the evening which kept the crowd moving their feet well into the night.

We hope you will join us for the 6th Annual Hearts for Holt Gala on Saturday, February 9, 2013. The gala is quickly becoming one of the most talked about events in Charlotte.

HOPE FOR HOLT
REACHING FOR A CURE

Photos in this article were taken at the 2012 Hearts for Holt Gala.

AUTHOR'S NOTE:

Kevin and I are the proud parents of Jenna and Patrick, age 7, who both have the genetic disease cystinosis. During the past 6 years, as the children have grown, we have been given the opportunity to provide regular updates for CRF newsletters and "Cystinosis Magazine." We are thankful for each chance we are given to make notes and observations about our family's life as our children live with cystinosis. I hope that the stories we provide help create awareness about cystinosis, while lighting the path for others who might learn from our experiences.

Special

Kids. Special Lessons.

By Teresa Partington
Jenna and Patrick's mom
Sacramento, California

The most recent "leg" of our journey with cystinosis occurred just last week. Jenna let me know over breakfast that she was hearing from children in her class that her breath was bad. Patrick, who always opts not to worry me, neither confirmed nor denied her observation.

I asked them if it would be okay for me to come to school and speak to the class a little bit about cystinosis; mostly about their medicine, which causes the smell of sulphur to be emitted from every pore of their little bodies all day long. Jenna thought it was a splendid idea, and she asked if she could help me present their story. Patrick would have preferred to skip the whole event, but bravely agreed that it would be okay. I felt that enlightening the class would make a difference because I believe children, given the opportunity, can grow to understand some of life's most complicated situations.

The kids' teachers allowed me to chat with the first grade class at Holy Spirit Parish School last Tuesday. I showed up with a few bottles of Cystagon®, the prescription medication they take, and let each of the kids take a whiff of the pills, which smell the same in the bottle as they do when they are metabolized by Jenna's and Patrick's bodies. With Jenna's help, I explained that: "Jenna and Patrick have cystinosis, which means their bodies were made in a special way. Each of us has something in our bodies called cystine. In the case of those with cystinosis, cystine has no means for escape from the body; so "smelly medicine" is taken, and it travels through the bloodstream, sticks to the cystine in Jenna's and Patrick's bodies, and carries it out!"

I also explained that "each of you will be going to school with Jenna and Patrick for many years. Now that I've taught you about cystinosis and their medicine, you can be a part of their health team! Whenever you smell the funny smell on them, please know that their medication is working, and they are staying healthy because of it. I have grown to love the smell – and perhaps you'll cheer for it too, since you know it's getting the cystine out and keeping your friends well!"

And with that I wrapped up a speech I had nervously anticipated for over five years. I noticed that Patrick nearly cried when I nearly cried, his empathy more powerful than cystinosis. Jenna continued to address the students, explaining that while Cystagon® smelled awful her other medicines tasted awful, but she took them anyway so she "could stay healthy," her verve more powerful than cystinosis. Other children were excited to share the medications they take – ranging from asthma treatments to vitamins and other drugs. Each of these explanations was important, helping J & P remember that others have burdens too.

I asked the kids at the end of the day if they thought the class meeting was good. Jenna said, "Mom, I think it worked!" She explained that she stood by her friend Vivian in the lunch line and Vivi (God bless her) said... "Jenna, I can smell that medicine on your body right now… and I'm glad!"

And with that, I truly felt we'd done the right thing.

Kevin and I and Jenna and Patrick would like offer our most sincere thanks to each of you who support Jenna & Patrick's Foundation of Hope. Thank you to loyal donors from Idaho, New Mexico, Washington and New York, and from all over the state of California! We thank the Cystinosis Research Foundation for taking on the precious funds JPFH raises each year, and for using every dollar given in the most discriminate, speedy and effective ways.

Sincerely, Teresa and Kevin Partington; on behalf of Jenna and Patrick and all who participate in cystinosis awareness and believe in a cure.

Originally published on the *ABC News* website.

For most of their young lives, Jenna and Patrick Partington have lived by the alarm clock – seven foul-tasting pills at 7 a.m., then again at 1 p.m., 7 p.m. and 1 a.m. If they are a little late or miss a dose, their bodies turn into time bombs, destroying every organ.

Cystinosis Kids Are Living Time

By Susan Donaldson James
ABC News

The 7-year-old twins from Sacramento, Calif., were born with cystinosis, a rare genetic disease that causes an amino acid, cystine, to accumulate in every cell of the body, damaging the kidneys, eyes, liver, muscles, pancreas, brain and white blood cells.

The only treatment is the drug Cystagon, which must be taken every six hours without fail, otherwise cystine dangerously accumulates in the body.

Without it, the average child will die of end-stage kidney failure by age 9. And even with treatment, many only live into their 20s and 30s.

"We take it day by day," said their father, Kevin Partington, 43, who works in commercial real estate. "I look at their pictures and they don't look that wildly different from their classmates. But the disease takes hold over a period of time."

Only about 300 to 500 patients in the United States have cystinosis – about 2,000 worldwide, according to the Cystinosis Research Foundation (CRF). Because it is a so-called "orphan disease," there is little financial incentive for pharmaceutical companies to find better treatments or a cure.

But today, the twins are among 41 patients who were part of phase-three clinical trials for a new formulation of the active ingredient in Cystagon that is time-released.

Raptor Pharmaceuticals will file with the Food and Drug Administration for fast-track approval of a new drug, RP103, this month. It could reach the market by the end of the year.

Patients can take the medicine every 12 hours instead of every six, no longer disrupting sleep and school.

It also has fewer side effects like nausea and gastric discomfort, because the medicine bypasses the stomach and goes directly into the duodenum.

"There's also more of a fudge factor," said Partington. "Before I would set the alarm for 1 and 7 and it beeped off and we were like Pavlov's dog. Now, it's breakfast and dinner time."

The CRF approached Raptor about marketing the drug, which was being developed at University of California, San Diego, to lengthen the time between drug doses. Scientists have seen a direct correlation between the difficult medication regimen and patient health outcomes.

"I was at a research meeting with a parent panel and they talk about the strategy around dosing meds," said Patrick Reichenberger, vice president of commercial operations for Raptor.

"Sunday night they have the syringes, the baggies, the day, the time mapped out for the whole week. I saw a table of the logistics. It's no wonder people miss doses because of the complexity."

Patients in the cystinosis clinical trials have reported less nausea, an increase in appetite and higher energy levels because they were not woken in the night. "Sleep deprivation is huge in growing kids," Reichenberger said.

The new drug is coated so it doesn't dissolve in the acidic environment of the stomach, but further in the intestinal tract.

RP103 is not a cure, but promising research is on the horizon. Stem cell and gene therapy are "the biggest source of our optimism," said Partington, the twins' father.

Diagnosis of the rare disease is one of the biggest challenges, according to Partington, because so few doctors have seen patients with the disease.

Bombs Without Meds

The twins were born on Dec. 7, 2004, slightly premature, but seemingly healthy. When they were around 6 or 7 months old, the babies began to drink "tons of water" and throw up.

"I've been around kids my whole life, and there is a difference between spitting up milk and a kid that looks like he's from *The Exorcist,*" he said.

Despite drinking constantly, their bowel movements were hard as golf balls and "actually hurt coming out," he said.

"We knew something wasn't right," said Partington.

The first clues came when Jenna went into the hospital for a severe flu. She was kept for two weeks, spending half the time in the pediatric intensive care unit. Her body had begun to cramp up with dehydration.

"I was changing her diaper and every time I pulled her legs down, she started crying," he said. "The doctor said she was a medical marvel – he couldn't figure it out."

The diagnosis of cystinosis was finally made in March 2006 by geneticists at Scripps Institute in San Diego, where much of the research on the disease is taking place.

Patrick's diagnosis followed after doctors tested for white blood cell cystine counts.

Both Partington and his wife Teresa carry a recessive gene for the disease. The twins are fraternal, so each independently has a 1 in 4 chance of inheriting both genes.

Odds were so rare of both children getting both genes, "We should have purchased a lotto ticket that day," said their mother Teresa Partington, 39, who has since dedicated her life to research and education through Jenna & Patrick's Foundation of Hope

Recently, she talked to the twins' classmates when Jenna said children had said her breath was bad. The medicine causes a rotten egg sulphur smell that emits from every pore.

"I felt that enlightening the class would make a difference because I believe children, given the opportunity, can grow to understand some of life's most complicated situations," said their mother.

Somehow, their children adapt to their treatment regimen. "The kids haven't known anything different," said Kevin Partington. "It's not perfect, but it's not as overwhelming as it was in the beginning. It's a routine as a family."

In addition to seven pills twice a day, they down a pomegranate-like cocktail of polycitric acid, iron, calcium, iron and vitamin K, among other ingredients. "It's terrible tasting," according to Partington. "But they shoot that down and go off to school."

All day they drink water and take bathroom trips every 35 minutes. Before bed they repeat the routine and though they don't have to be woken for another pill now, they are up to use the toilet.

"Usually, they pee a lot in their sleep and we have to change them," he said. "If we woke them up every time, they wouldn't sleep. Their beds are wet every morning."

Patrick was found to have high cholesterol and so both children are now on statins, which their parents fear can cause memory loss.

As it is, they struggle with spatial and visual deficits, which are part of the disease. Since starting school, they are showing some dyslexia.

"Physically, they are not as vital as other kids," said their father.

"Hydration is a big problem and in Sacramento when it gets to 100 degrees ... they don't sweat," he said. "Sports like soccer are not an option – they'd wilt like flowers. But they are able to keep up."

The biggest challenge is psychological.

"It's really hard for us – they are our only two kids," said Partington. "We can't compare them to other kids we've raised.

"We don't know when they're not doing their homework if they don't get it like any other kid, or because of the cystinosis. Or are they just being precocious 7-year-olds playing their mom and dad. There are so few cases out there to share those ideas with."

But his wife says, raising their twins, despite the odds, is "ultimately rewarding."

"We strive to teach our kids and those around us that a person can rise above just about anything by treasuring what's important and doing good," she said. "I would choose happy kids over healthy, though I never imagined I would have to make such a choice."

For more information or to help, go to Jenna & Patrick's Foundation of Hope at www.jennaandpatrick.org or the Cystinosis Research Foundation at www.cystinosisresearch.org

Originally printed in February 1, 2012 edition of The Charlotte Observer

Mom's Persistence Got Correct Diagnosis

Now she raises money for rare disease her son is fighting

By Amy Reiss

Holt Grier and his mom, Chrissy, watch the stars.

Years ago, Chrissy Grier walked down the hallway of her home in Huntersville, towel in hand, and caught sight of her 1-year-old, Holt, in the bathtub. For many parents, the scene of a toddler in a tub, warm and rosy-cheeked, would send a shiver of contentment down their spine.

For Chrissy, a different thought flashed through her mind.

She thought: My son is dying.

His body is frail, his skin translucent. His shoulder blades and bones and ribs are evident enough to be individually counted. He looks like a child you'd find on the pages of *National Geographic*. He looks like he's starving to death.

That day in the fall of 2006 marked the beginning of a five-year journey for Holt, Chrissy and the Grier family – a journey that's far from over. There were misdiagnoses, challenges and tears, and along the way a correct diagnosis for Holt – cystinosis – and a calling for Chrissy, as she attempts to fight not only for her son, but others affected by this rare and potentially fatal disease.

Because cystinosis is so rare, Holt's diagnosis was not an easy one. He presented with symptoms of excessive thirst, vomiting and constipation. The Grier's pediatrician began with a diabetes test that showed that Holt was leaking sugar into his urine. None of his symptoms added up. The doctor was gravely concerned, but had to send them home without answers. That night, Chrissy saw him in the tub ... and her gut told her something was really, really, wrong.

She called the next day, insisting on bringing Holt to the hospital for a full work-up. The hospital said they'd call with the results.

They did call, at 8 o'clock that night. And Chrissy will never forget what they said.

"You need to come here, now. Don't change his clothes, just get in the car and drive downtown. There's a bed waiting. His potassium levels could cause heart failure," the doctor said.

"There's panic," Chrissy said. "And you go into this strange, maternal, adrenaline fight mode."

The Griers spent the next two months seeing specialists, none who could piece together the strange puzzle that was Holt's symptoms. He was tested for cystic fibrosis, as well as a litany of other diseases – so many that Chrissy can't begin to name all of them.

"At one point, we brought the city out to test the creek behind our house and see if it had any mercury, to rule out mercury poisoning," she remembers.

As time progressed, Holt got worse and worse. His muscles deteriorated, he was sick and listless with no appetite. Chrissy's pediatrician suggested a nephrologist.

"Of course, they wanted us to wait for weeks. I said, 'I can't afford to do that,' so we went to the office the next day and just waited for hours for someone to see us," she said.

Who they did see was Dr. Charles McKay – and Holt greeted him by projectile vomiting all over the man. But by the end of the day, the Griers had some answers. McKay felt very strongly that Holt had Fanconi syndrome, the result of the genetic disorder cystinosis, a lysosomal storage disease. The disorder causes the accumulation of the amino acid cystine within cells. Left untreated, the disease causes complete kidney failure, muscle deterioration and blindness. And there is no cure.

The long road began for the Griers, beginning with treatment with a sulphur-based medicine that was tortuous to administer every six hours. After months of stress associated with getting a 22-month-old to choke down a foul-tasting medicine, the Griers decided to have a gastric feeding tube put in his stomach. Over time, Holt's energy levels improved, the vomiting slowly disappeared, and his appetite increased. He started physical and occupational therapy to learn to pull up and eventually walk.

Now six and part of the Montessori program at Davidson Day School, Holt still faces challenges, but he is happy and making progress every day. In December, he became part of a study testing a new medication administered every 12 hours instead of six, and Chrissy is blown away by the effect on him. "He is a different child because of it," she said.

Chrissy and her husband, Jason, now live in Cornelius, along with Holt, their daughter Mary Logan, 11, and son Jack, 9. They started the Hope for Holt foundation back in 2007, with 100 percent of proceeds going to cystinosis research. Feb. 4 will mark the fourth annual Hearts for Holt gala at the Myers Park Country Club. It will include a silent auction, food and dancing.

"We have hope," she told me, "and that's huge."

BLESSED

By Bryan Stout
Lincolnton, North Carolina

My name is Bryan Stout. I was diagnosed with cystinosis/Fanconi syndrome at 18 months of age. I later developed rickets. Because of my condition many people, even so called professionals, tried to convince my parents that I should be treated differently, possibly even home-schooled. Fortunately, my parents disagreed and I was brought up just like my siblings. Of course, I was the smallest but, I got along just fine.

Because of kidney failure I started dialysis around the age of nine. My mom learned how to operate the dialysis machine at home so we wouldn't have to travel three times a week. She would also give me injections when I was a child. We always said that mom should have been a nurse.

I remember her wrapping plastic bags around my stomach so that I could enjoy the ocean with the rest of the kids. People stared but it was so worth it! I really didn't have any major complications with the dialysis.

Finally, after 2½ long years of waiting, we received a call from Duke University. Days later I got the best gift ever, a new kidney – it was a blessing! I remember all the nights we spent at Duke very well. I healed pretty quickly and actually felt better within just a few days. My dad kept me laughing every time the doctors would leave the room. I truly believe that having a sense of humor and staying positive are two of the most important aspects of life.

My siblings, Amelia, Maygen and Grayson have also played an important role in my life. They have all helped me by reminding me to take my numerous medications. They have provided a lot of moral support for me, especially when I had to receive an emergency tracheostomy when I was 16. Because of all my previous surgeries, doctors decided the breathing tubes had caused scar tissue that lead to difficulty breathing. I lived with the trachea for almost seven years before I found a fantastic surgeon. After six surgeries he removed the trachea.

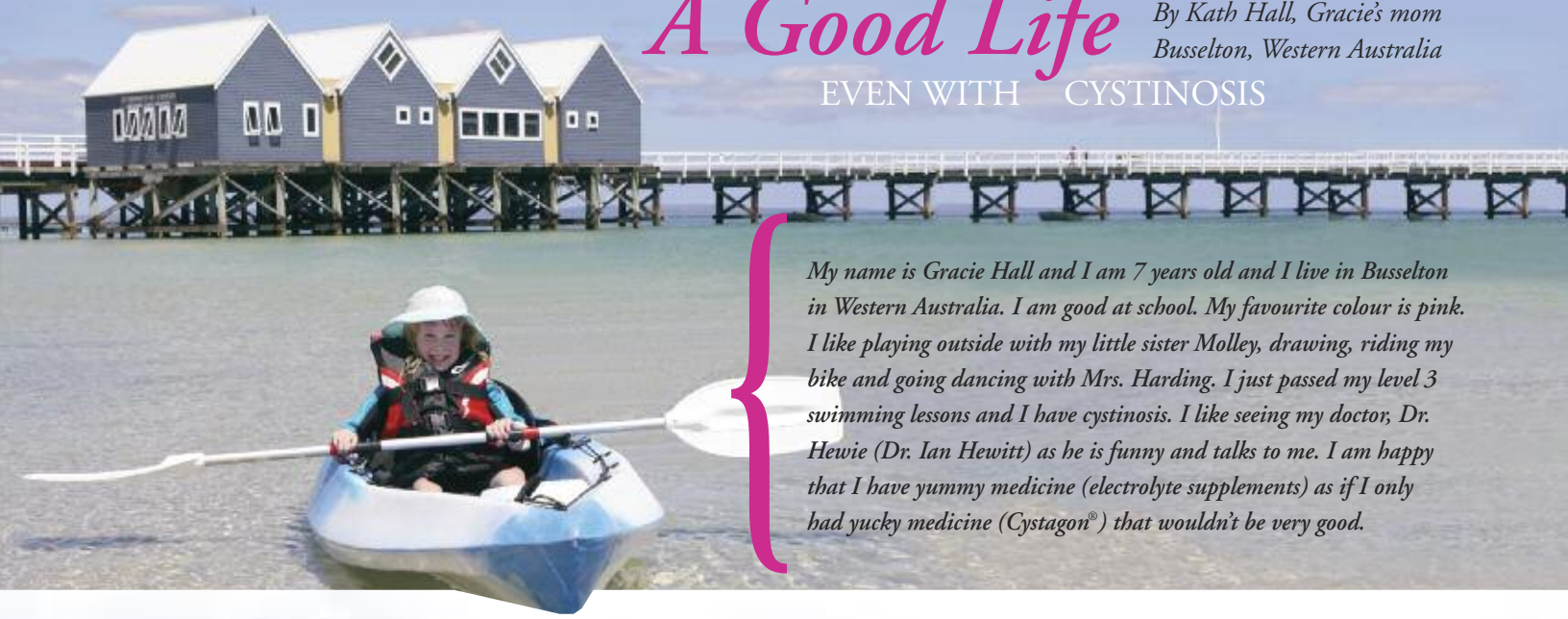
It was very difficult being a young adult with such an obvious medical problem. But, I believe that God doesn't give us anything that we can't handle. It is amazing what doctors and prayers can do.

Today I am healthy and as of February 18, 2012 I will celebrate the twentieth year of having my kidney! I love football, anything outdoors, I enjoy working out, spending time with my family and I like to cook.

Be thankful for what you have and count your blessings daily, it could always be worse. God Bless.

A Good Life
EVEN WITH CYSTINOSIS

By Kath Hall, Gracie's mom
Busselton, Western Australia



My name is Gracie Hall and I am 7 years old and I live in Busselton in Western Australia. I am good at school. My favourite colour is pink. I like playing outside with my little sister Molley, drawing, riding my bike and going dancing with Mrs. Harding. I just passed my level 3 swimming lessons and I have cystinosis. I like seeing my doctor, Dr. Hewie (Dr. Ian Hewitt) as he is funny and talks to me. I am happy that I have yummy medicine (electrolyte supplements) as if I only had yucky medicine (Cystagon®) that wouldn't be very good.

As Gracie's mum. I smiled at her comments on having cystinosis. Like many special children she has an amazing positive attitude despite the many challenges of living with a chronic disease. At seven she is starting to realise that she is a little different. I am not sure how she will feel as she gets older, but it is a journey that we are all on together.

As are all families, we were devastated when we learnt that Gracie had cystinosis. Our smiley happy baby was diagnosed with rickets and failure to thrive just after her first birthday. It was another six months before the confirmation of cystinosis became our reality. Our little world turned upside down. My husband's response was to research all he could find on cystinosis, armed with information and knowledge on how to manage her condition. Mine was to deal with the day-to-day issues and not look too far ahead, different coping strategies that we still both use.

Like other families with children with cystinosis our "normal" life is structured around medicine, doctors' appointments and fear of gastro. Not many people know of Gracie's illness, not that we don't want to share it, it's just that it doesn't come up in conversation very often. I am not sure if this is the right way to go, but in a way we have 'normalised' cystinosis so much that we almost think it is normal. I think as Gracie gets older and understands her condition more, our 'normal' may change.

For the moment she is a happy, well-adjusted little girl. She has just started year two and loves school. Despite being told in kindergarten that she would probably need a full-time aid, she hasn't yet, and passed year one with flying colours. Life is busy with dancing and swimming lessons, surf club and going to the beach.

Most of the time life is good, but like all families, we have some tough times. I sometimes wonder if cystinosis is the reason we have some of our challenges. I have realised though it doesn't really matter. Cystinosis is part of who Gracie is and we love her for who she is.

We are both nervous and excited about the future. The progress made by cystinosis researchers in the last few years has given us real hope. Our hope, as with all cystinosis families, is for a cure so we are eternally grateful to the wonderful people raising funds and researching cystinosis. In the meantime we take each hurdle as it comes and enjoy the 'normal' times in between.

Darren, Gracie, Molly and Kath Hall

Joshua Clarke

By Rose Clarke, Joshua's mom
Garden Grove, California

Joshua was diagnosed with cystinosis in January 2008. It is amazing to look back at pictures of him at 15 months of age before his diagnosis and to look at him now. He is now a thriving 5-year-old, doing extremely well and keeping very busy. He continues to grow and gain weight and is steadily moving up the growth charts. Joshua has begun school and is attending a two-year kindergarten program at the school where his siblings attend. He is progressing very well and has begun to read simple sentences.

Joshua currently takes eight different medications a day, every six hours. In addition, he is injected nightly with growth hormone and continues to receive occupational and physical therapy for his developmental delays. He has made incredible progress with his eating difficulties; he has increased his volume and is actually finishing small portions of food. He continually asks for food and is trying new foods and textures. He is, however, still unable to eat enough to sustain himself. He relies on his G-tube for his nutritional needs and medications.

Joshua remains a loving, spirited and joy-filled little boy. His positive energy keeps our family smiling and laughing. Joshua enjoys Tae Kwon Do, building with Legos©, reading books and has recently begun playing baseball. He has been blessed with two siblings who always play with him and take excellent care of him. Joshua is a wonderful helper around the house, enjoys dancing (especially during baseball games!) and is counting the days until he can become a Scout like his brother and sister.

Three and a half years ago our lives changed forever. In the months that followed Joshua's diagnosis, we were without hope and knew only despair. We have certainly come a long way. We realize that there are many challenges that lie ahead. Recently, we were faced with our first challenge that was not medical in nature. As a result of fear and lack of knowledge about his condition, and more specifically his G-tube, Joshua was dismissed from school in September 2011, after only two and a half weeks of attendance. The school could not explain why he was dismissed except to say that it did not have the appropriate personnel to handle his condition and therefore his enrollment presented a liability for the school. We were devastated. This school was home to Joshua's siblings and he was very well-known and loved by lots of other students.

The outpouring of support for Joshua and our family that followed was overwhelming. In many instances, perfect strangers were ready and willing to help in any way they could. In a situation that seemed hopeless, a community came together to bring hope to a little boy and his family. Equally important, this community and school administration received education about a rare condition known as cystinosis. In the end, we came to an understanding and Joshua has returned to school, and is having a wonderful time.

With the help of the Cystinosis Research Foundation, Joshua and our family are extremely hopeful. We are not immune to worries for the future: hourly eye drops to dissolve painful crystals, renal transplantation, and a host of other related organ malfunctions. Each day we pray that the life-saving medication, Cystagon®, will continue to prolong his life and prevent the horrible effects of this disease from causing Joshua any further damage.

We are very thankful for all those involved with the Cystinosis Research Foundation and the incredible strides they have already made. We are confident that a better quality of life and a cure are on the horizon for all cystinosis patients.

Thank you for your support of our family, *Joshua's Journey of Hope* and the Cystinosis Research Foundation.

The G-Tube Question

Tina Flerchinger
Clarkston, Washington

By Dennis Arp

Early in her family's fight against the scourge that is cystinosis, Denice Flerchinger arrived at a bridge she was determined not to cross. But once she took the first step, she never once looked back.

Like many parents of a cystinosis child, Denice and Mark Flerchinger agonized over whether they should take the route of the G-tube. Having a gastric feeding tube surgically inserted in their daughter, Tina, would normalize her nutritional intake and make it easier to administer medications around the clock. But the Flerchingers worried that once Tina got on the tube, she might never come off.

Ultimately, the disease made the decision for them.

In a time when most kids grow rapidly, 10 to 17 months, Tina lost weight. "She was extremely frail and weak. She couldn't walk without holding on to something," Denice said. When the final diagnosis of cystinosis was finally given, the team of specialists told Denice and Mark that Tina would not survive without a gastric tube.

The G-tube was a part of the Flerchingers' lives for about six years, and Denice now calls it the best decision they ever made, with regard to Tina's health.

"It saved Tina's life," she said without hesitation.

The Flerchingers' experience offers a window into one of many difficult decisions cystinosis parents face. Every case is different, Denice emphasized, and every family has to make their own decision based on the best information available.

"But I have never spoken to a single person who said, 'Oh, I wish we hadn't gone through with this,' " she said. "For Tina and for our peace of mind, the G-tube was definitely the right choice."

That peace of mind proved elusive during the seven months that it took to get an accurate diagnosis of Tina's condition.

Once it was determined Tina's ailment was cystinosis, the Flerchingers came to grips with the reality that their child had a debilitating disease for which there was no cure. When they started the life-sustaining course of treatment, they found that the challenges were only beginning.

"In the beginning Tina was taking 11 medications," Denice said. "A healthy child could not even do this without great difficulty, and a child with cystinosis doesn't want to eat, which only complicates things."

The screaming and crying, the nausea and vomiting, the nutritional deficiencies, the stress of holding Tina

The Flerchingers faced a difficult choice, and have never regretted their decision.

Photo by Lars Wanberg

> *It makes me appreciate the good days she does have, embracing them and taking each day one at a time.*

down to get her to eat or take her meds, only to have one or both come back up – it all added up to a scenario many parents of cystinosis patients would find all too familiar.

However, that familiarity doesn't make it easy to endure. And when it became clear that the G-tube was necessary, the family moved quickly to adapt.

The new "routine" included Tina having the tube in her abdomen and a feeding pump in a pack she wore on her back during the day. After she started gaining weight, and her electrolytes were stabilized with the right balance of meds, they switched to night feeds only. "Night feeds can be difficult. More often than not, Tina would wake up vomiting. There is that perfect balance of getting enough nutrition, but too much will cause stomach upset," Denice said. "We would sneak in throughout the night to give meds through her tubing, and cross our fingers that she wouldn't wake up." Although the G-tube brought its own set of complications, a new sense of normalcy and stability entered the Flerchingers' lives.

The site of the incision was prone to infection, bloody and raw due to acid backing up into the tube from the stomach. Seepage would leak through Tina's shirts and cause her consternation. Then there was the constant accumulation of tubing, feed bags and syringes that needed to be cleaned and filled.

However, all of that was secondary to Tina's weight gain, health improvement and acquisition of new stores of resiliency.

"She couldn't wait to go to school and show her second belly button," Denice said. "That was always her show-and-tell the first day of school. We have always told her God made her special and she was proud to be unique in her own way."

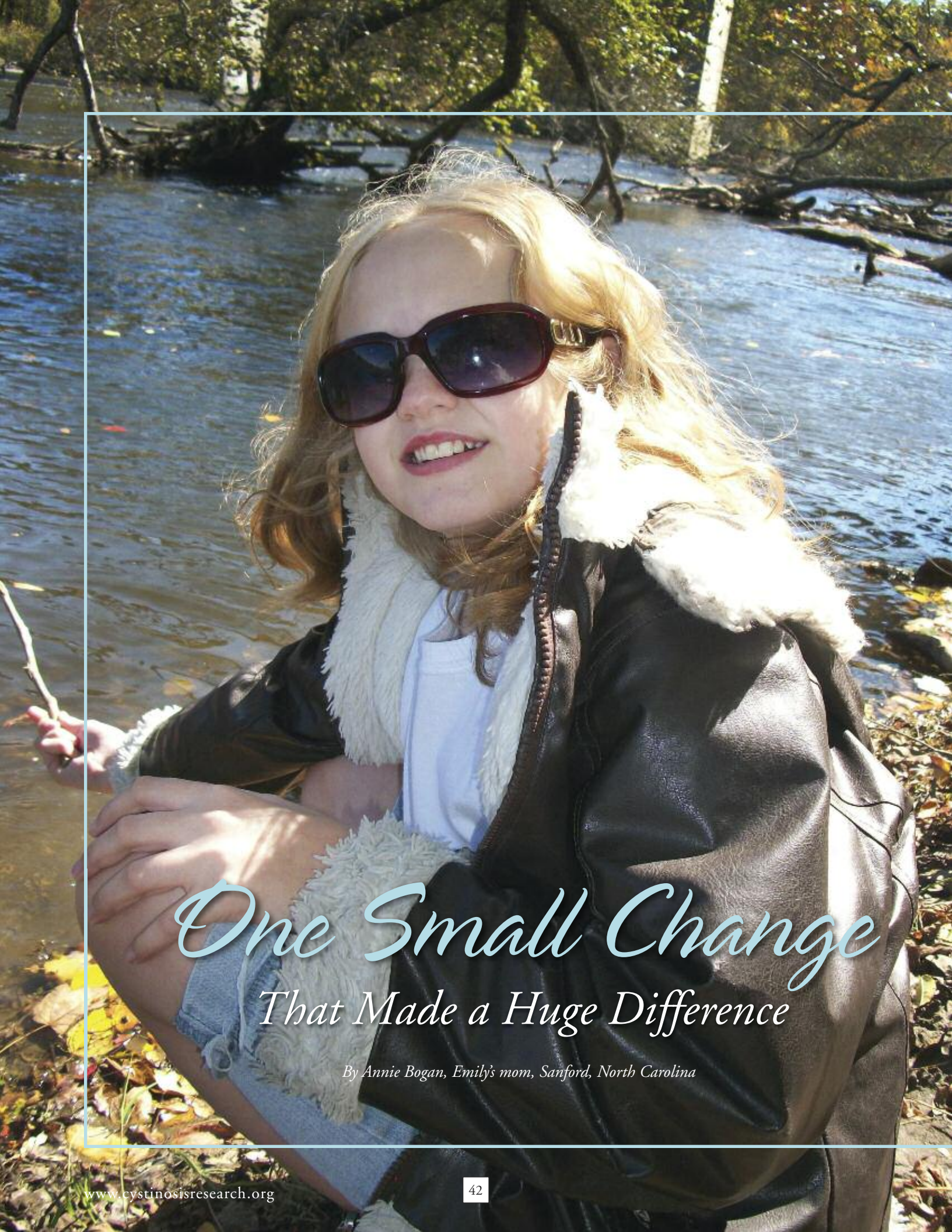
Although Tina no longer has a G-tube, the family still spends one day a week washing syringes and refilling them with meds for the week. It is a time of unity, solidarity and equanimity within the family.

"There is one mom who gathers her girlfriends together and they make a party of it. It actually becomes fun."

For Tina, treatment is hardly fun, but the 8-year-old is doing well her mom said. She is able to eat and take her medications without the constant companion of nausea and vomiting.

On those occasions when Tina doesn't feel good, "it reminds me of when she NEVER felt good," Denice said. "How wonderful it is not to have that anymore."

"It makes me appreciate the good days she does have, embracing them and taking each day one at a time."



One Small Change
That Made a Huge Difference

By Annie Bogan, Emily's mom, Sanford, North Carolina

Emily was diagnosed with cystinosis in 2001. After taking Cystagon® for several years, she was invited to participate in the delayed-release cysteamine study in late 2010.

Emily's story mirrors most within the cystinosis community. Around her first birthday, she began to fall off the growth chart, crave water and stop eating. I frantically grasped at straws, trying to find the culprit of her symptoms. Finally, she received a diagnosis at 22 months of age.

The relief of putting a name with her condition was quickly snuffed out by the trauma of forcing her to take Cystagon®. More times than not, Emily would vomit within half an hour of taking the medication. It was a vicious cycle: take pills, vomit, repeat … over and over. It was common for the process to take hours. As it was, by the time a dose had been successfully given (and kept down), it was time to start the brutal regimen again.

Reluctantly, I succumbed to the reality that Emily would require a G-tube for her life-sustaining medications. Our days became filled with doctor visits, hospitalizations and projectile vomit.

Looking back, that chapter of our lives seems like a bad dream. I do not know how we survived but it is my suspicion that it was only by God's merciful grace.

Now, fast forward …

In 2010, I did a happy jig (literally) when I received an email from the Children's Hospital of Atlanta saying Emily was accepted into the delayed-release "RP103" trial.

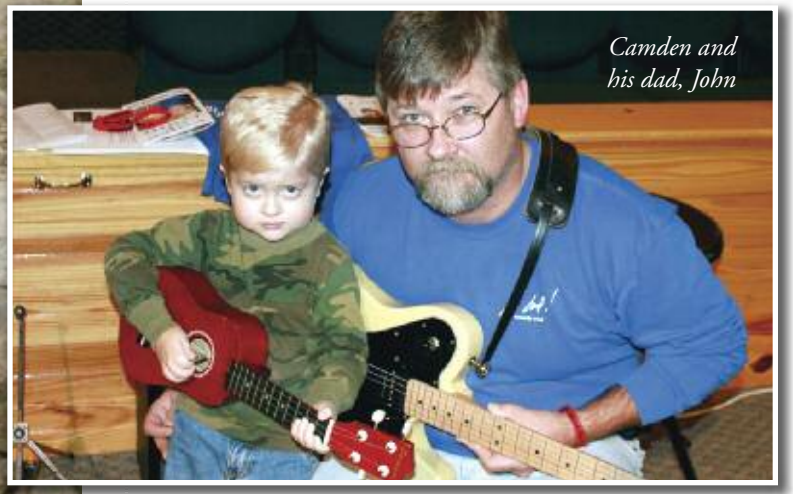
For over a year, I insisted Emily take her Cystagon® pills by mouth so she would be an acceptable candidate for the study. At that time, participants were required to take the medication orally. I gladly accepted the task of making 20 initial visits to Georgia, in hopes of finding a more plausible lifestyle for Emily – one that would more easily carry into her teen and young adult years – and one that would make her feel more normal and less like she was living life in six-hour increments.

Emily has been taking RP103 for over a year now and, while it has been life-altering to get a full night's sleep, the unforeseen effects of the medication have been an even greater blessing. Because she no longer has the horrid nausea that accompanied her 6 a.m. Cystagon® dose, our mornings are much more pleasant and I now drop a happy little blonde 7th grader off at middle school each morning.

Less nausea also equates to better compliance with Emily's other medications, resulting in better labs all-around. Finally, and of the most value, Emily's cystine levels have consistently been below 1.0 since she began RP103 – proving the medication is working and, hopefully, minimizing the destruction caused by cystinosis throughout her body.

We are forever grateful to Raptor, its sponsors, the Cystinosis Research Foundation and everyone "behind the scenes" who have made this study possible. While we all know there is much, much more to be done in our fight against this vicious disease, we know this drug will make our wait for better treatments – and, hopefully, a cure – more bearable, realistic and "normal."

Camden, 6 and his brother Colin, 3



Camden and his dad, John

Camden getting meds through his G-tube

Camden

By John Sanders, Camden's dad
Gordon, Georgia

Camden started on RP103 on November 18, 2011, and it has been a blessing. Once we got the right recipe for pushing it through the stomach tube it has done very well. I had to increase the size from a FR14 to a FR16 but after that it was smooth sailing.

Camden still throws up once or twice a month but he is trying to control it so that it does not become a habit. He still gets tired but not like before RP103. I see big improvements in his energy level and eating habits, and overall I can tell he feels better.

After we learned how to get the RP103 through the tube I asked the doctors to put him back on the Potassium Micro-K, which is time-released and not as harsh on the GI tract.

We held our fundraising event on March 3, 2012 and it turned out fairly well considering the weather. We didn't raise as much as last year but we are still proud since every dollar counts when it comes to research. The Akins again did a terrific job with entertainment, and our silent auction was great. I would like to thank Sue and Serena Scott from Australia who made and donated items for our auction. Sue and Serena are wonderful people. I also had a great volunteer staff this year. Without them it would have been impossible.

Of course, the most special help comes from MAMA. She always dives in and does whatever is needed. She is the shoulder I cry on and she is always there for me.

I am looking forward to the cure and with funding I think we will find it. CRF is working with outstanding doctors and scientists. For those who do not believe the cure is around the corner, you will be happily surprised when that day comes.

Matthew Hawkes

My name is Matthew Hawkes. I am 25 years old and I live in a small town called Weston in England. I was diagnosed with cystinosis at four months old when my parents discovered that I had a massive thirst for water.

At first, doctors thought that I might be just one of "those babies" but how they were wrong! And my parents, like most people, were unaware of this condition and didn't expect me to live the normal life I do today.

I was signed over to a renal doctor at Southmead Hospital where I was under the watchful eye of a renal team until I had a kidney transplant at the age of 16.

I would say my childhood memories are like any other normal person aside from the tubes, disgusting medication, growth hormone injections, and many stays in the hospital, which became like a second home to me!

Throughout school I had a support worker, who I hated at first because it made me so different from everyone else. Now I realize that life would have been much harder without help taking medication, falling behind with school work, and my support worker trying her hardest to keep my enthusiasm up.

I had lots of friends in school and although most of the time I suffered from exhaustion, severe sickness and side effects from all the medication, I got into as much trouble as my other friends, if not more!

My teenage years – when my friends became aware of how things were different for me and started asking questions – were the hardest for me. Staying at friend's houses was always a big issue since I was drip-fed and on dialysis, which meant that my parents would come to collect me as late as possible to keep me as normal as everyone else.

Being a teenager with cystinosis was one of the toughest times of my life but it helped me become the person I am today and helps me realize how important it is to live life to the fullest and enjoy every moment.

In April 2002, I was transplanted with a kidney kindly donated by my mum. My dad was the better match but we discovered that he had high blood pressure. That was a very crazy time for me as the local press got involved and I ended up on the front page of my local newspaper and in television headlines. I never did it but I was even asked to be a guest on a daytime TV program.

I remember how well and full of life I felt within a day of having my transplant. My appetite was enormous, which was really strange since I'd never had one before. My cheeks got chubby and my eye brows became really bushy, which I was told was a side effect from the anti-rejection drugs, but soon went back to normal. About six months after my transplant I had one major rejection, so I had to go under the knife again for a kidney biopsy and was given a large dose of steroids. The steroids returned my kidney function to a reasonable level. Since then I've had no major rejections and my anti-rejection drugs have been reduced to a smaller dose although my Cystagon® capsules have increased to 350mg four times a day.

My life has changed so much since having my transplant and I'm a totally different person with no tubes and no disgusting medicines to take. Still, I have my good and bad days when it is difficult to stay energized and enthusiastic at work and when I'm with friends.

Being a teenager with cystinosis was one of the toughest times of my life but it helped me become the person I am today and helps me realize how important it is to live life to the fullest and enjoy every moment. I am also thankful to my mum for the life I live today.

Henry and his friend Rowen playing superheroes

Henry and Sam Jenkins at the Stanford RP103 clinical trial

A very happy Henry

Photo by Staci Bailey

Henry Sturgis:

Staying Busy and Growing Stronger in Beautiful Northern Idaho

Henry has made great progress this winter. He was accepted into the delayed-release drug trial and has been taking RP103 since November and is doing much better. He has fewer side effects such as vomiting and is less tired.

Our overall med schedule is a little less frequent, which allows for more flexibility, sleep and normalcy. Henry takes his own kidney medicines at the afternoon dosing. That gives him some independence and control. His kidney-related labs have remained at good levels and we were able to reduce his Poly Citra medication.

Although Henry is still thin for his age he has grown much taller this year. He is now in the 50th percentile, partly due to the daily growth hormone injection he receives.

We now give him his nightly injection when he is sleeping soundly, and it works much better and is less traumatic on everybody in the house. We tried this method about a year ago, but it didn't work very well. We revisited the method last summer and Henry actually asked to have his shot like that every night.

Henry is 5½ now and will turn 6 on July 19. He is currently in preschool and will start kindergarten in the fall. He has been able to cut down his therapy a little, especially speech, which has really improved over the last couple of years. With longer preschool hours this year, we were too taxed going to multiple therapy appointments, so we now just do one half-hour session through the school district.

Summer will allow for different kinds of activities such as summer camp, church camp or possibly some intensive physical or occupational therapy that can be condensed for a summer schedule.

Henry is learning to snow ski again this winter and is really making strides. He is good enough to take off his edgy-wedgies, (a strap that keeps the ski tips together), and is relying on his leg-muscle strength. He likes running into his buddies on the ski hill or in the lodge at lunch. Henry also loves Superheroes and Harry Potter.

He is still not a big eater but he loves the lodge hamburgers with ketchup and a cookie. This is always followed by chocolate Boost Plus, his typical meal at home. We have experimented with probiotics and fiber, which have given his immune system a boost and have helped him with illnesses at school.

As parents of a child with health issues, we wear many hats and we have many daily chores such as laundering of bedding each morning, purchasing and preparing meds, reading and understanding lab reports, coordinating medical appointments and working with teachers. Henry has an Individualized Education Plan through the school district, which gives us some choices in public schools.

We ask our family and friends to help us with different tasks regularly, and we are very grateful for their help and support.

We hope everyone is looking forward to spring and the many bounties it provides. We can't wait for the sun to return to Northern Idaho.

THE STURGIS FAMILY, SANDPOINT, IDAHO

DAY of HOPE

Cystinosis Research Foundation Family Conference

Thursday, April 19 – Saturday, April 21, 2012

Balboa Bay Club, Newport Beach, California

The 2012 *Day of Hope Family Conference* will take place over three days and culminate on Saturday night at the Tenth Annual Natalie's Wish Celebration, *Wishes, Heroes and Miracles*.

Learn • Laugh • Share • Celebrate

The conference will focus on the progress CRF-funded researchers have made over the past several years. Sessions will include:

- Research news about stem and gene therapy
- Novel eye treatment research progress
- Research updates related to kidney disease
- Update on the effects of muscle wasting
- Quality-of-life research study results
- Cystinosis and the brain
- Update on the RP103 (delayed-release cysteamine) clinical trial
- Report on the Cure Cystinosis International Registry (CCIR)

SCHEDULE

Thursday, April 19
Check-in at the Balboa Bay Club
Welcome reception and family dinner

Friday, April 20
Conference sessions
Followed by a family dinner celebration

Saturday, April 21
Conference sessions

Saturday evening plan to join us at our **Tenth Annual Natalie's Wish Celebration, *Wishes, Heroes and Miracles*.**

All families are encouraged to participate in the discussions and question and answer sessions. Families will have a chance to meet, socialize and share their personal stories of life with cystinosis.

Hotel Information – Balboa Bay Club and Resort
www.balboabayclub.com ✭ Toll free (888) 445-7153
1221 West Coast Highway, Newport Beach, California 92660

We have secured a special flat rate of $175/night for cystinosis families. Visit the reservation site https://roomres.balboabayclub.com/bbc/?requesttype=invBlockCode&code=CYSTINOSIS1204

If you contact the hotel via phone be sure to mention CRF Group/Block code Cystinosis1204.

For more information, contact Nancy Stack at nstack@cystinosisresearch.org or Stacy Johnson at (949) 223-7610 sjohnson@cystinosisresearch.org.

CYSTINOSIS RESEARCH FOUNDATION

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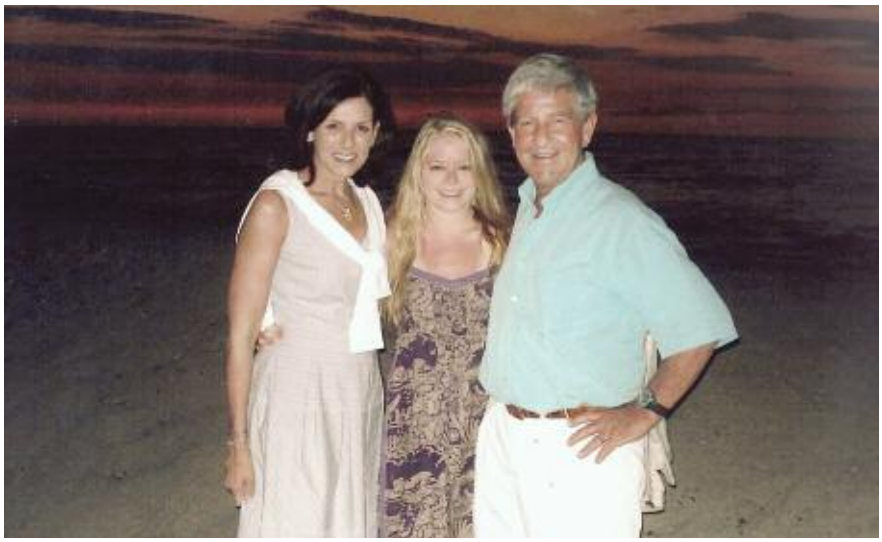
FROM A DAUGHTER'S WISH TO A MOTHER'S MISSION



The Stack family: Nancy, Natalie and Jeff

When Nancy Stack's daughter Natalie was diagnosed with cystinosis as an infant almost 20 years ago, all the information she had on the rare, or orphan, disease was in a short pamphlet from the hospital.

Cystinosis, a disease where cystine crystals develop and eventually destroy the major organs, was considered to be terminal with very limited treatment options.

Natalie's 12th birthday wish was "to have my disease go a way forever." That wish prompted Nancy and her husband Jeff to found the Cystinosis Research Foundation (CRF) in 2003. "Our mission was to create a dynamic, ongoing cycle of cystinosis research, so this orphan disease would not be left behind," says Stack. Today, CRF has raised nearly $16 million for research grants and funded more than 84 cystinosis studies, giving hope and support to families affected by the disease around the world.

Two grants have been awarded for studies on corneal cystinosis to Gavin Herbert Eye Institute doctors Jennifer Simpson, MD, Associate Clinical Professor of Ophthalmology, and James Jester, PhD, Professor of Ophthalmology and Biomedical Engineering.

"Together, the Gavin Herbert Eye Institute and the Cystinosis Research Foundation are helping create treatments for children with cystinosis here and all over the world," says Stack. "Natalie is proud of the CRF grants that help bring treatment and hope to the entire family of people with cystinosis."

For more information on CRF news and events, read the cystinosis research article on the following page and visit www.cystinosisresearch.org.

Originally printed in the fall 2011 edition of *Shine the Light,* a publication of

THE GAVIN HERBERT EYE INSTITUTE
UNIVERSITY of CALIFORNIA • IRVINE

FOR TREATING CYSTINOSIS

How do you treat a disease so rare that it only affects about 2,000 people in the world? Jennifer Simpson, MD, Associate Professor of Ophthalmology at the Gavin Herbert Eye Institute, and Cystinosis Research Foundation (CRF) founder Nancy Stack are working toward finding treatments and a cure for cystinosis.

Cystinosis most commonly affects children and adolescents in the corneas, kidneys and the brain – causing blindness, renal failure and even death. The disease occurs when the body accumulates the amino acid cystine, a building block of proteins, which forms damaging crystals that appear during childhood and adolescence. Oral medication called cysteamine can reduce the crystals in the kidneys and other organs, but has no effect on reducing corneal crystals that cause pain, corneal scarring and loss of vision. No meaningful treatment currently exists for corneal cystinosis.

A Clear View

Dr. Simpson and Nancy Stack first met at a UC Irvine-sponsored cystinosis luncheon in 2007. Hearing Stack's account about the frustration over limited corneal cystinosis therapies, and also about a newly developed cystinosis mouse model, Dr. Simpson realized how she could help. "Research and progress in rare diseases like cystinosis are often hampered by the difficulty in gathering enough patients to study and understand the disease. An animal model would give us an opportunity to test novel treatments and potentially accelerate research on cystinosis."

This led Dr. Simpson to approach her Gavin Herbert Eye Institute colleague James Jester, PhD, the Jack H. Skirball Endowed Chair of Ophthalmology and Professor of Biomedical Engineering at UC Irvine. As a renowned expert in corneal imaging, Dr. Jester would be able to study cystine crystal formation in the mouse model using high resolution 3D photographs.

Using an animal model, Jennifer Simpson, MD, works on treatments for a rare eye disease.

In a CRF-funded study using the animal model, Dr. Simpson and Dr. Jester were able to precisely show the progression of corneal cystinosis. The crystals form early in life and fill the corneas, which results in light sensitivity, eye pain, debilitating glare and inflammation that leads to corneal scarring and blindness. Establishing how corneal cystinosis progresses was a huge milestone that has been shared with other researchers around the world through the CRF International Symposium.

"We now have a more complete understanding of the disease process, instead of just a snapshot," says Dr. Simpson. "Being able to visualize the crystals, see where they accumulate and follow them over time allows us to determine if a new therapy is actually working, and much more quickly than if we had to extract and extensively process the tissue."

Setting Their Sights

Building on their findings, Dr. Simpson and Dr. Jester are currently investigating the effectiveness of new therapies including stem cells, which can potentially replace the corneal cells filled with cystine crystals. They are also working on new ways to deliver cysteamine eye drops, which currently have to be put into the eye every hour of every day.

"Long-lasting eye drops with a timed release could reduce this frequency, making cysteamine treatment more realistic for children and teenagers with corneal cystinosis," explains Dr. Simpson.

"None of this would have been possible without the many opportunities for collaboration at the Gavin Herbert Eye Institute," says Dr. Simpson. "By partnering with foundations, eye care companies and other institutions, we are working to deliver the best therapies for our patients. The freestanding eye institute that is now being built will further support these efforts by keeping physicians and researchers in close proximity. It will give us momentum when developing new therapies to treat people with both rare and common eye diseases."

Originally printed in the fall 2011 edition of *Shine the Light,* a publication of

THE GAVIN HERBERT EYE INSTITUTE
UNIVERSITY of CALIFORNIA · IRVINE

Story reprinted courtesy of

LEWISTON TRIBUNE

It's Official!

GENO BONNALIE NOW HOLDS THREE GUINNESS BOOK WORLD RECORDS

Before Tuesday morning, Geno Bonnalie was confident that he had played more holes of golf in one week than anyone in history.

But when official confirmation of his record came in the form of an email from the Guinness World Records organization, it did give Bonnalie a extra boost of satisfaction.

"Obviously it's much cooler to have Guinness say, 'Yeah, you have the record,'" the 27-year-old Lewiston man said Tuesday evening. "Once I got that, I was pretty pumped."

Bonnalie set the record in late June/early July, when he scrambled through 2,000 holes over the course of seven days at the Lewiston Golf and Country Club. He played as many as 18 rounds in a day, and passed the old record of 1,801 holes.

Bonnalie also set two other world records during his quest that speak to his skill as a golfer. He notched 493 birdies and, in one 12-hour period, 67 birdies.

Those records have not yet been confirmed. Bonnalie had to submit additional paperwork for those marks, and he was told that approval could come later this week.*

Bonnalie didn't submit documentation of his record until November, mostly because he was tracking down statements from "50-some" witnesses who took turns monitoring him around the course. He also had to create a highlight video of his record chase.

And then he waited nearly three months before getting a congratulatory email from Guinness on Tuesday.

"I had heard stories of them being just really brutal in assessing a record," he said. "I was a little bit concerned that I may had missed something, but I read through all the documentation that they required several times and triple-checked my information. I was pretty confident that it was going to happen."

When Bonnalie completed his quest on July 3, his hands were ravaged by blisters and his right knee was sore. He said he doesn't plan on staging another golfing marathon until his record is broken.

"I hope this holds up for a little while, anyway," he said. "If somebody beats this, my hat's off to them, because I know how hard it was."

Geno with his now 8-year-old cousin Tina Flerchinger.

He did it to raise money for cystinosis research.

Bonnalie paired his record pursuit with a fundraising effort for the Cystinosis Research Foundation, which is searching for treatments and a cure for the rare disease, which Bonnalie's cousin, 8-year-old Tina Flerchinger, has suffered from her entire life. He ended up raising more than $15,000 for cystinosis research.

For more information about cystinosis and ways to donate visit www.cystinosisresearch.org or www.tinashopeforacure.org.

**All three of Geno's records have now been confirmed by Guinness World Records organization.*

FORE A CURE GOLF TOURNAMENT RAISES $218,000 FOR RESEARCH


Jeff Stack with Billy Skeffington, president of Ben's Asphalt of Orange County.

On November 14, 2011, a sold-out field of golfers, sponsors, underwriters and other donors helped the Cystinosis Research Foundation raise more than $218,000 for cystinosis research on a perfect day for golf at the Santa Ana Country Club. There were 148 golfers, 47 sponsors, a beautiful private golf course and fantastic weather. *Who could ask for more?*

There were many past sponsors and golfers at this year's tournament, as well as many new golfers playing in their first Fore a Cure tournament. We are grateful to everyone who participated for their commitment to Natalie's Wish and joining us in our quest for a cure.

The day began as players checked in and received their "goodie bags" – Quiksilver duffle bags filled with special gifts including a Carnoustie golf shirt; a bottle of Pinot Noir provided by Zotovich Cellars; a sleeve of Titleist ProV1 golf balls from Manly & Stewart; a Fore a Cure ball marker provided by Gramercy Gifts; and water courtesy of Independence Bank. Each golfer was also fitted for Foot Joy golf shoes.

On the course, the players participated in contests including a *Putting Contest, Longest Drive, Closest to the Pin* and *Straightest Drive*. Fabulous *Hole-in-One* prizes were provided by Fletcher Jones Motorcars and Traditional Jewelers of Newport Beach. Special thanks to our hole sponsors: Champion Fire Systems, Eagle Construction, Contractors Flooring, NASA Services, CB Richard Ellis Capital Markets, Ben's Asphalt, SARES•REGIS Group, Nelson Paving and Foto Cabina.

Following the tournament, players enjoyed cocktails and hors d'oeuvres during a silent auction and opportunity drawing that netted more than $11,900. After a delicious steak dinner, the live auction raised $33,450.

Thanks to tournament chairman Vince Ciavarella and his extraordinary committee:
Art Barrett, Ron Dyer, Jaime Henry, Robin Jochims, Stacy Johnson, Bill Keller, Samra Keller, Jill Manly, Marylyn Milburn, Mike Raring, Don Solsby, Zoe Solsby, Jeff Stack, Nancy Stack, Mike Winter and Amy Yovan.

Thank you to our sponsors, underwriters and supporters

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Joe McKay, Tournament Chair Vince Ciavarella, Mike Wolfe and Mike Wood

Steve Craig, Thad Foret, Jeff Stack and Billy Skeffington

Dr. Ranjan Dohil, Brian DeRevere, Peter Rooney and John Hagestad

2011 CRF Autumn Grants Funded

Total: $776,693

Angela Ballantyne, PhD,
Principal Investigator
Doris Trauner, MD,
Co-Principal Investigator
Dept. of Neurosciences,
University of California San Diego
"Patient-Reported Outcome and Health-Related Quality of Life in Adults with Cystinosis: A Study Utilizing the NIH "PROMIS"
$51,260 – 1-year grant

Stephanie Cherqui, PhD, Mentor
Brian Yeagy, PhD, Research Fellow
The Scripps Research Institute,
La Jolla, California
"Stem and Gene Therapy for Cystinosis"
$72,503 – 1-year grant

Francesco Emma, MD,
Principal Investigator
Bambino Gesú Children's Hospital
and Research Institute, Rome, Italy
Maria Antonietta De Matteis, MD,
Co-Principal Investigator
Telethon Institute of Genetics and Medicine,
Naples, Italy
"Drug Library Screening to Improve the Outcome of Nephropathic Cystinosis"
$323,150 – 2-year grant

Elena Levtchenko, MD, PhD,
Principal Investigator
Department of Pediatric Nephrology,
University Hospitals Leuven, Belgium
Maria Antoniette De Matteis, MD,
Co-Principal Investigator
Telethon Institute of Genetics and Medicine,
Naples, Italy
"The Role of Altered Calcium and mTOR Signaling in the Pathogenesis of Cystinosis"
$258,500 – 2-year grant

Tara McMorrow, MD,
Principal Investigator
University College Dublin, Ireland
Philip Newsholme, PhD,
Co-Principal Investigator
Biomedical Sciences, Curtin University,
Perth, Western Australia
"Role of Nitric Oxide in the Kidney Proximal Tubular Dysfunction Associated with the Fanconi Syndrome in Cystinosis"
$71,280 – 1-year grant

CRF — Lay Abstracts — Autumn 2011 Grants

Stephanie Cherqui, PhD, Mentor
Brian Yeagy, PhD, Research Fellow

Project Title: Stem and Gene Therapy for Cystinosis

Objective/Rationale: Our previous work has shown that stem cell based gene therapy in a cystinotic mouse model is effective in treating cystinosis. The three major mechanisms under investigation for this type of stem cell based treatment are cellular differentiation, cell fusion, and cell-cell interactions. It is the objective of this project to determine the major factors involved in the fusion process.

Project Description: The basis of our approach will be using both a mouse model and in vitro cell culture to investigate what factors are contributing to the stem cell fusion process. The cystinotic mouse model we developed has dual fluorescence that distinguishes the host cells (red) from the transplanted cells (green). The host/donor-fused cells in several organs will be easily recognized (yellow) and thus isolated to further study them to determine what kind of genetic and other biological factors are involved. The cell culture experiments will allow us a more controlled environment to further test the finding we get from the mouse model.

Relevance to the Understanding and/on Treatment of Cystinosis: Gaining a better understanding of the mechanism of the stem cell-based treatment in our model for cystinosis will give us a better grasp of why this treatment is so effective. This is important for the stem cell therapy for cystinosis, and for the regenerative medicine in general.

Anticipated Outcome: This project will enable us to determine the major genetic factors related to the process of cell fusion between the host and donor cells in our mouse model. By identifying these factors we hope to be able to gain a more selective understanding of their function by using cell culture experiments.

Elena Levtchenko, MD, PhD, Principal Investigator
Lambertus van den Heuvel, PhD and Antonella De Matteis, MD, PhD, Co-Principal Investigators

Project Title: The role of altered calcium and mTOR signaling in the pathogenesis of cystinosis

Objective/Rationale: Despite the fact that the molecular basis of cystinosis due to the deficiency of cystinosin has been described more than 13 years ago, the mechanism of the disease still remains obscure. Generalized dysfunction of renal proximal tubules (called renal Fanconi syndrome) usually develops during the first year of life and progresses towards end stage renal failure before the age of 10 years. The administration of cysteamine postpones the deterioration of the renal function and protects extra-renal organs, however, renal Fanconi syndrome, when established, is resistant to cysteamine therapy. Recent findings have pointed to the processes that can be disturbed in cystinotic cells beyond lysosomal cystine accumulation, among them, the process of autophagy and endoplasmic reticulum (ER) stress. In this project we aim to study these new mechanisms in more detail. In particular, we will focus on the role of disturbed Ca and mTOR signalling in cell dysfunction in cystinosis.

Project Description: This project will be carried out on immortalized proximal tubular cells obtained from urine of healthy volunteers and cystinotic patients. We will also use cystinotic cells rescued with a functional *CTNS* gene and healthy cells with down-regulated *CTNS*. In these cells will first study the altered autophagy and related to it mTOR signalling pathway, using standard methods. We will investigate both direct effect of *CTNS* gene dysfunction on mTOR and its indirect influence through altered endocytosis observed in cystinotic cells. Next, we will study ER and lysosomal calcium fluxes in control and cystinotic cells to find out the cause of altered calcium signalling and its relation to altered autophagy and enhanced ER stress.

Relevance to the Understanding and/or Treatment of Cystinosis: Many cystinosis patients suffer from proximal tubular dysfunction that cannot be effectively cured by the existing treatment. In this project we aim to test several compounds influencing mTOR and Ca signalling for restoring renal cystinotic phenotype *in vitro.*

Anticipated Outcome: We expect to unravel the underlying mechanisms of altered autophagy and enhanced ER stress in cystinosis and to find out whether the cystinosis phenotype can be ameliorated by restoring calcium and/or mTOR signalling.

Angela Ballantyne, PhD, Principal Investigator
Doris Trauner, MD, Co-Principal Investigator

Project Title: Patient-Reported Outcome and Health-Related Quality of Life in Adults with Cystinosis: A Study Utilizing the NIH *"PROMIS"*

Objective/Rationale: The objectives of the proposed study are to (1) gather vital information on patient-reported outcome and quality of life in the ever-growing population of adults with cystinosis, and (2) gather information on the final illnesses and specific causes of death in adults who had cystinosis and passed away during the past 10 years. This information can then be used as one method to weigh risks vs. benefits of emerging therapies, such as stem-cell therapy.

Project Description: Study participants will be at least 50 adults (ages 18 and older) diagnosed with cystinosis. (The goal is to obtain as many adults as possible, ideally more than 50.) This age group has been selected in order to examine outcome and quality-of-life in these individuals now that they are surviving well into adulthood. This study will utilize a computerized online questionnaire, the *Patient-Reported Outcomes Measurement Information System (PROMIS)*. The PROMIS was developed as part of the NIH's 21st century "Roadmap" for medical research, and is well validated and normed.

An additional subject group will be included as an ancillary part of this study. Participants will be at least 20 parents (or nearest living relative) of individuals with cystinosis who died within the past 10 years. Information on the patient's final illness and cause of death will be gathered from parents/relatives.

Relevance to the Understanding and/or Treatment of Cystinosis: Findings of the proposed study will contribute a quality-of-life dimension to the fund of intensive research needed to consider stem cell therapy as a viable treatment approach for cystinosis. Moreover, the data will serve as a baseline from which future treatments/clinical trials for adults with cystinosis can be launched.

Anticipated Outcome: The advent of renal transplantation and cysteamine therapy have served to extend the lifespan of individuals with cystinosis into adulthood, but they do not prevent the ultimate progression of the disease. For this reason, it is important to learn about the longer-term effects of cystinosis on quality-of-life in adults with the disease, as well as the final illnesses and causes of death in this population. This knowledge can then be used in the planning of and/or justification for emerging therapies and treatments for adults living with cystinosis.

Tara McMorrow, MD, Principal Investigator
Philip Newsholme, PhD, Co-Principal Investigator

Project Title: Role of nitric oxide in the kidney proximal tubular dysfunction associated with the Fanconi syndrome in cystinosis

Objective/Rationale: Oxidative stress (derived from excessive superoxide and hydrogen peroxide production) is a key component of kidney proximal tubule dysfunction in cystinosis. Glutathione, a major intracellular anti-oxidant has recently been shown (in the laboratory of Dr Elena Levtchenko and published in BBA 1812: 643-651) to be increased in concentration following Cysteamine treatment, leading to protection but not full recovery of the cystinotic cells.

We believe, based on pilot studies performed in UCD Dublin, that nitric oxide, (a free radical that causes damage in cells) is generated at elevated levels in cystinotic kidney proximal tubule cells leading to cell dysfunction. Our objectives are thus to define the levels of nitiric oxide generated in cell models of cystinotic cells and to determine the targets of nitric oxide action and the downstream consequences of nitric oxide associated protein modification.

Project Description: We will determine nitric oxide levels and concentrations of nitric oxide modified proteins in various models of cystinotic kidney proximal tubule cells. In addition we intend to measure markers of oxidative stress including reduced and oxidized glutathione levels and cell energy status.

We will determine the level and activity of the key enzyme generators of nitric oxide and superoxide in the normal vs cystinotic cell models. We will additionally measure the levels and activity of key functional markers of proximal tubule cells, the sodium transporters Na+/K+ATPase and the Type 3 Na/H exchanger.

We will additionally use a state of the art 'proteomics' facility available in the Conway Institute, UCD Dublin, to determine the level of 'nitric oxide' modified proteins in the various cystinotic cell models.

Lastly, we will attempt to reduce levels of protein modification by nitric oxide using pharmacological inhibitors, if the modification is deemed to have a negative effect on cell function

Relevance to the Understanding and/or Treatment of Cystinosis: The project may reveal novel therapeutic targets for the future treatment of kidney malfunction in cystinosis.

Anticipated Outcome: We anticipate initial discovery of the proteins modified by excessive nitric oxide (and perhaps superoxide) generation in cystinotic cells and as such determine novel pathways that lead to kidney proximal tubule cellular dysfunction in the disease of cystinosis.

2012 Call for Funding Proposals

The ultimate goal of the Cystinosis Research Foundation is to find a cure for cystinosis. Global calls for grant and fellowship applications are announced bi-annually in March and September. Research and fellowship awards will be given for up to 3 years. The number and value of the awards will depend on the number of outstanding proposals received and the value of the funds available at the time.

The CRF announced its Spring 2012 call for proposals on March 12, 2012. Currently, CRF has more than $1.1 million available for new grants. The deadline for applications is April 23, 2012. New research grants and fellowship will be announced in July 2012. **Visit www.cystinosisresearch.org/For-Researchers for details.**

CRF Science Report and Research Grant Updates

CRF research grant progress reports are published in the *Research* section on our website: www.cystinosisresearch.org. As updates are received they appear in our monthly *Star Facts* e-newsletter.

Studies Published by CRF-Funded Researchers

Cysteamine Restores Glutathione Redox Status in Cultured Cystinotic Proximal Tubular Epithelial Cells – *BBA,* June, 2011 by Elena Levtchenko, MD, PhD, University Hospital, Leuven, Belgium; Martijn Wilmer, PhD, and Lambertus P. van den Heuvel, PhD

Mechanism of Proton/Substrate Coupling in the Heptahelical Lysosomal Transporter Cystinosin – *The PNAS early edition,* January, 2012 by Bruno Gasnier, PhD, CNRS Research Director, Université Paris Descartes, Paris, France

Cysteamine Therapy: A Treatment for Cystinosis, Not a Cure – *Kidney International,* January, 2012 by Stephanie Cherqui, PhD, Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, CA

Transcriptional and Posttranscriptional Regulation of the *CTNS* Gene – *Pediatric Research,* February, 2011 by Francesco Emma, MD, Division of Nephrology and Dialysis, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy

Analysis of CTNS Gene Transcripts in Nephropathic Cystinosis – *Pediatric Nephrology,* March, 2010 by Francesco Emma, MD, Anna Taranta, PhD, Department of Hephrology and Urology, Division of Nephrology, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy

Modulation of CTNS Gene Expression by Intracellular Thiols – *Free Radical Biology & Medicine,* January, 2010 by Francesco Emma, MD, Anna Taranta, PhD, Department of Hephrology and Urology, Division of Nephrology, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy

CYSTINOSIS RESEARCH FOUNDATION

International Symposium a Huge Success

THIRD INTERNATIONAL Cystinosis Research Symposium

The Third CRF International Cystinosis Research Symposium concluded just as this publication was going to press.

The conference, organized and underwritten by the Cystinosis Research Foundation, and sponsored by Raptor Pharmaceuticals, Sigma-Tau Pharmaceuticals, Inc., and CheckOrphan, attracted 60 leading researchers and scientists from seven nations. Participants gathered at the Arnold and Mabel Beckman Center of the National Academies of Engineering and Science in Irvine, California, to share information about their research and exchange ideas about promising new study directions, all with the goal of finding better treatments and ultimately a cure for cystinosis.

Four prominent scientists were the conference co-chairs: **Corinne Antignac, MD, PhD,** Hôpital Necker-Enfants Malades, Paris, France; **Stephanie Cherqui, PhD,** The Scripps Research Institute, La Jolla, California; **Julie Ingelfinger, MD,** Harvard Medical School, Boston, Massachusetts; and **Elena Levtchenko, MD, PhD,** University Hospital Leuven, Leuven, Belgium. Their many hours of detailed planning was evident throughout the two-day event.

Jeff and Nancy Stack, founders of the Cystinosis Research Foundation, welcomed guests on Thursday morning. **Jerry Schneider, MD,** the symposium's honorary chair and chair of the previous two conferences, provided the opening remarks.

Pierre Courtoy, MD, PhD, Head of Cell Biology Unit & Platform for Imaging Cells and Tissues, Université catholique de Louvain, de Duve Institute, Brussels, Belgium, gave the keynote address on Thursday morning, and **Donald Kohn, MD,** Professor, Microbiology, Immunology and Molecular Genetics and Pediatrics at UCLA and a member of the CRF Gene Therapy Consortium gave the keynote address on Friday morning.

One new and highly popular feature of the conference was a poster session featuring 11 invited scientists who presented their research studies to all attendees.

On Thursday evening, the CRF Scientific Review Board was honored for their tireless work on behalf of the cystinosis community. Their expertise and leadership ensures that CRF funds only the most promising research studies. The board is comprised of chair **Corinne Antignac, MD, PhD,** Paris, France; **Stephanie Cherqui, PhD,** La Jolla, California; **Allison Eddy, MD,** Seattle, Washington; **Francesco Emma, MD,** Rome, Italy; **Julie Ingelfinger, MD,** Boston, Massachusetts; **Elena Levtchenko, MD, PhD,** Leuven, Belgium; and **William Rizzo, MD,** Omaha, Nebraska.

The openness and camaraderie, sometimes rare at scientific conferences, created a sense of excitement that was palpable as the researchers returned to their labs throughout the world.

Many attendees claimed that the synergy in the cystinosis research community, is a direct outgrowth of the CRF funded symposia.

A more complete report of the conference proceedings will be included in the next issue of *Cystinosis Magazine*.

Cystinosis Research Foundation

We are indebted to everyone who serves on a Cystinosis Research Foundation Board for their leadership, guidance and commitment to helping our children.

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MISSION

The mission of the Cystinosis Research Foundation is to support bench and clinical research that is focused on developing improved treatments and a cure for cystinosis.

EDUCATION

The CRF is dedicated to educating the medical and public communities about cystinosis to ensure early diagnosis and proper treatment.

SCIENTIFIC REVIEW BOARD

The Scientific Review Board is composed of leading cystinosis scientists and experts from around the world. Members are actively involved in the grant review process, evaluating and analyzing all research proposals submitted and advising the CRF on the scientific merit of each proposal.

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CYSTINOSIS
RESEARCH FOUNDATION

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CURE CYSTINOSIS INTERNATIONAL REGISTRY

The Cure Cystinosis International Registry (CCIR) is a collaborative effort by the leaders in the cystinosis community to establish a comprehensive, global patient registry for cystinosis. The purpose is to connect those with cystinosis to the research community in an effort to find a cure for cystinosis.

CCIR BOARD OF ADVISORS

The CCIR Advisory Board is dedicated to promoting and facilitating current research and medical information to the global cystinosis community in an effort to inform the community of current treatments, clinical trials and studies and patient care.

Bruce A. Barshop, MD, PhD
University of California, San Diego

Kyle Brown, CEO, Innolyst, Inc.

Betty L. Cabrera, MPH
University of California, San Diego

Paul Goodyer, MD
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Nancy Stack, Cystinosis Research Foundation

Jody Strauss, Cystinosis Awareness and Research Effort

Tricia Sturgis, 24 Hours for Hank

Doris A. Trauner, MD
University of California, San Diego

CCIR MEDICAL AND SCIENTIFIC COUNCIL

The CCIR Medical and Scientific Council was instrumental in the development, design and content of the medical questionnaire for the registry. The Council provides ongoing guidance relating to the scientific and clinical aspects of the registry.

In addition, Dr. Barshop, Dr. Goodyer, Dr. Schneider and Dr. Trauner are members of the *Ask An Expert* sub-committee that addresses questions from cystinosis patients.

Bruce A. Barshop, MD, PhD
University of California, San Diego

Stephanie Cherqui, PhD
The Scripps Research Institute, La Jolla

Ranjan Dohil, MD
University of California, San Diego

Paul Goodyer, MD
Montreal Children's Hospital, Canada

Daniel R. Salomon, MD
The Scripps Research Institute, La Jolla

Jerry Schneider, MD
Dean for Academic Affairs, Emeritus
University of California, San Diego

Doris A. Trauner, MD
University of California, San Diego

www.cystinosisregistry.org

CYSTINOSIS RESEARCH HOLDS THE POTENTIAL TO HELP MILLIONS WORLDWIDE

"Cystinosis is a metabolic disease that belongs to the big family of lysosomal storage disorders. These diseases often affect children and result in progressive multiple organ dysfunction and severe clinical complications. Developing new therapies for cystinosis will provide insights to approaches that may have general applications for these diseases."

STEPHANIE CHERQUI, PHD, THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

"Seven years ago CRF went out on a limb to fund a series of studies that would not have received funding from conventional sources. These studies resulted in the development of EC-cysteamine, and ultimately the Raptor Pharmaceutics RP103 formulation. These new formulations have helped make cysteamine easier to ingest and tolerate, and as a result have opened the door for treating other diseases with this, as yet, underused drug.

"A pilot study published earlier this year has shown that cysteamine may be a potential new therapy for the epidemic non-alcoholic liver disease (NASH). A multicenter Raptor Pharmaceutics study is being considered next year for the treatment of NASH."

RANJAN DOHIL, MD, UNIVERSITY OF CALIFORNIA, SAN DIEGO

"We wouldn't be where we are in this process today without CRF. Their support led to the proof of concept and this new formulation (RP103)."

TED DALEY, PRESIDENT, RAPTOR PHARMACEUTICAL CORP.

"In our recent CRF-funded research studies that were designed to provide new insights into the question of why cysteamine has been so effective in preventing chronic kidney disease in patients with cystinosis, we have discovered that it reduces kidney scarring – a universal process of kidney destruction that mediates all chronic kidney diseases. If these findings are confirmed with further studies, they would provide rationale for testing the efficacy of cysteamine as a treatment for many other forms of human kidney disease.

"Currently it is estimated that 13–16 percent of all adults in the United States have chronic kidney disease (that is, with renal function less than 60 percent of predicted normal levels) and is associated with five-fold increased risk of premature death due to accelerated cardiovascular disease. New therapies are urgently needed for this large patient population."

ALLISON EDDY, MD, SEATTLE CHILDREN'S HOSPITAL, SEATTLE, WASHINGTON

"Corneal cystinosis offers several advantages as a model from which therapies for more prevalent eye diseases will also benefit. First, since the genetic defect has been identified, the disease mechanism is well understood. Second, there is now a well-characterized animal model that can be used to evaluate new therapies. Finally, while the number of affected patients is relatively small, cystinosis affected individuals and families are highly motivated and well organized, making them an excellent population for the orphan drug and device program at the U.S. Food and Drug Administration.

"Examples of such potential cross-over benefits include the use of stem cell transplantation and long-acting drug delivery systems. While both of these approaches are being developed for corneal cystinosis, they also have tremendous potential in other ophthalmic conditions. These include, corneal chemical burns, which results in corneal scarring; corneal surface dysfunction, which causes severe dry eye; and a number of conditions that require chronic drop therapy, most notably glaucoma and uveitis. With the well-defined clinical endpoint of reduced crystals, corneal cystinosis provides valuable scientific and regulatory validation for novel therapeutic approaches to these more common conditions."

JENNIFER SIMPSON, MD, UNIVERSITY OF CALIFORNIA, IRVINE

This copy was originally published in the fall 2011 issue of *Cystinosis Magazine.*

TOGETHER WE ARE MAKING A DIFFERENCE. SAVE THE DATES

NOT YOUR FATHER'S (or Mother's) FUNDRAISER







Friday, April 13, 2012
Celebrating Abigail Mary Monaghan's Birthday
Sunglasses Day at Oakridge Public School
St. Catharines, Ontario, Canada

Saturday, May 5, 2012 ★ 11 am
Cystinosis Awareness and Research Effort – Gabbie Strauss
3rd Annual Lance Roberts Shredding Party to Cure Cystinosis
Waterloo, Ontario, Canada

Monday, May 14, 2012 ★ 5:30 pm
Cystinosis Awareness and Research Effort – Gabbie Strauss
Treat Yourself Spring Fashion Show
Creekside Campus, Waterloo, Ontario, Canada

Saturday, May 19, 2012 ★ 6 pm
Tina's Hope for a Cure – Tina Flerchinger
Fourth Annual Wine, Stein & Dine
Rogers Toyota Scion Showroom
Lewiston, Idaho

August 2012
Cystinosis Research Foundation – Natalie Stack
Crash and Crush for a Cure sponsored by Ben's Asphalt
Orange County Fair – Demolition Derby
Costa Mesa, California

September 2012
Joshua's Journey of Hope – Joshua Clark
On-Line Auction – Donations are welcome
Contact Marianne Clarke, clarkema@verizon.net

Saturday, September 8 – Sunday, September 9, 2012
24 Hours for Hank – Henry Sturgis
24 Hour Bike Ride –
Cycling for Cystinosis
Sandpoint, Idaho

Friday, October 5, 2012
Jenna & Patrick's Foundation of Hope – Jenna and Patrick Partington
Swing and Bling Event
Teal Bend Golf Club and The Citizen Hotel
Sacramento, California