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MEDICAL BREAKTHROUGHS IN THE BLUEGRASS

MORE INSIDE

- Some adults with sickle cell disease feel their needs are not being met in Louisville. **A9**
- An experimental study is letting a Louisville man wean himself off anti-rejection drugs — and their side effects — after a transplant. **A10**

WEB EXTRAS

At www.courier-journal.com/research:

- An interactive timeline on medical innovations in Kentucky.
- How blood cells take on a sickle shape that clogs blood vessels.
- Video of Terrell Starks, a dying 23-year-old sickle cell disease patient, and his family.
- Parts 1 and 2 of Medical Breakthroughs in the Bluegrass.

WHAT'S COMING

Spring: Advances in spinal-cord research at the universities of Louisville and Kentucky.
Late spring: Advances at U of L and UK in cancer research, especially lung cancer.

By Sam Upshaw, The Courier-Journal

Valicia Starks clutches son Terrell Starks, who is dying of sickle cell disease at their home in Shively.

By Sam Upshaw Jr., The Courier-Journal

Amos Igwe, 13, has sickle cell disease but is no longer plagued by symptoms after receiving an experimental bone marrow transplant from his sister Chi-Chi Igwe, 8.

U of L researcher may hold key to a CURE FOR SICKLE CELL

By Laura Ungar
lungar@courier-journal.com
The Courier-Journal

It strikes thousands of African Americans every year, clogging blood vessels with sickle-shaped cells — causing strokes, blindness and excruciating pain as it damages the heart, liver, lungs and kidneys.

Half of its victims die by age 40.

But University of Louisville researchers are testing a revolutionary cure for sickle cell disease, giving hope to a new generation of families that carry the potentially fatal gene.

Amos Igwe, 13, believes the procedure has given him a future.

Before getting a bone-marrow transplant from his sister in 2006 as part of the experiment, Amos was often so sick that he had trouble breathing and could barely leave the living room couch.

Today he plays quarterback on a football team at St. Albert the Great, where he's an eighth-grader, is preparing to go to Trinity High School next year and hopes to one day become a dentist or heart surgeon.

"We are grateful to God," said his father, Tony Igwe of eastern Louisville. "It's really a miracle."

Amos was one of six patients treated as part of a study that aims to make bone-marrow transplants safe enough to be used widely and possible beyond the small portion of patients with perfectly matched donors. Such transplants can potentially cure sickle cell disease, but are considered too dangerous in most cases because they can lead to deadly complications such as graft-versus-host disease, in which a donor's cells attack the recip-

See **SICKLE CELL**, A8, col. 1

MEDICAL BREAKTHROUGHS IN THE BLUEGRASS

ABOUT THE SERIES

In the past decade, researchers at the University of Louisville and the University of Kentucky have helped the state become a growing center for globally significant medical breakthroughs.

They aim to save and change lives by working to heal the heart with stem cells from fat, detect Alzheimer's before it steals minds, help the paralyzed walk and cure the devastating sickle cell blood disease.

The research boom was jump-started by Bucks for Brains, a multimillion-dollar initiative the state launched in 1998 that has brought top researchers to state universities. A decade of public and private investment is starting to pay dividends, offering hope in one of the nation's most unhealthy states.

In an occasional series, The Courier-Journal explores groundbreaking medical research at U of L and UK.

In September, the newspaper looked at work at U of L's Cardiovascular Innovation Institute. In November, we examined the latest Alzheimer's research at UK. Today, we look at U of L research that could lead to a cure for sickle cell disease, an inherited disorder that targets African Americans.

SICKLE CELL | U of L researcher may hold key to cure for deadly disease

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ient as foreign.

Dr. Suzanne Ildstad, research leader and director of U of L's Institute for Cellular Therapeutics, is attempting to overcome such complications by inducing a patient's tolerance to the donor cells.

She said study results are promising — with two of six patients basically cured and a third recent one doing well — and it shouldn't be long before new, safe transplants are available to many of the nation's 70,000 sickle cell patients.

"Amos was one of our first two successes," said Ildstad, whose team is collaborating with Duke University. "He's making normal red cells. He grew more than a foot in the past year. ... He's living a normal life."

By Sam Upshaw Jr., The Courier-Journal

Dr. Suzanne Ildstad, research leader and director of U of L's Institute for Cellular Therapeutics, says results are promising — with two patients basically cured and a third one doing well.

Central to Ildstad's work is her discovery in 1994 of a "facilitating cell" in bone marrow, which helps stem cells in a donor's marrow to "take" in a recipient, lessening the chance that the patient's immune system will reject the donor cells.

Safe bone-marrow transplants may also offer new treatments for conditions such as Type I diabetes and multiple sclerosis, she said, and a better approach to organ transplants that doesn't require a lifetime of anti-rejection drugs.

Ildstad's research has sparked excitement among scientists across the nation and has attracted ongoing funding of up to $7 million a year to U of L from such organizations as the National Institutes of Health, the U.S. Department of Defense and the National Foundation to Support Cell Transplant Research.

But not everyone is certain that Ildstad has found a widespread cure for sickle cell disease. Dr. John DiPersio, chief of oncology at Washington University in St. Louis, said it's unusual that her results haven't been replicated by many other teams, and that there hasn't been more follow-up on facilitating cells.

"I think she's a little on the fringes here," DiPersio said.

Ildstad countered that other researchers have studied these cells, which have also been the subject of numerous medical journal articles and international talks. And Dr. Joanne Kurtzberg, a Duke collaborator on the project, said skepticism accompanies "every new innovation in the field."

To Amos, Ildstad is a champion.

"I used to have trouble breathing. Now I'm gaining some muscle. I can play basketball with my friends. I can jump high," said the teen, who stands 5 feet 4. "She made all this happen. I feel like I'm cured."

'MIXED CHIMERISM'

Blending two systems of bone marrow into one

In Ildstad's office are images of the chimera, a mythical creature with a lion's head, a goat's body and a serpent's tail. It symbolizes the premise of her work — "mixed chimerism," in which two bone marrow systems exist and function in one person.

Ildstad, a 57-year-old married mother of two grown children, graduated from Mayo Medical School in Minnesota, trained in Harvard University's general surgery program and was a staff fellow at NIH. It was there that she helped establish a model for a blood stem-cell chimerism, in which two genetically different stem cell populations coexist.

One of her most well-known and controversial efforts took chimerism to the extreme. In 1995, while at the University of Pittsburgh, she won federal approval to give a 38-year-old AIDS patient a transfusion of baboon bone marrow with added facilitating cells. While the marrow didn't take, the patient's health improved.

But the procedure was heavily criticized, with some scientists worrying it could introduce baboon viruses into humans.

Ildstad also applied the idea of chimerism to sickle cell disease. In the United States, the inherited condition is most common among those of African descent, and is marked by defective hemoglobin, the oxygen-carrying protein in red blood cells.

Patients' red cells carry less oxygen than normal, and many are shaped like crescents, or sickles, instead of doughnuts. The misshapen cells don't move easily through tiny blood vessels, causing clogs and resulting in terrible pain and damage to such organs as the kidneys, brain and heart.

Ildstad reasoned that a safe bone-marrow transplant could halt this destructive cycle by helping patients make normal red blood cells. And chimerism, achieved with the help of facilitating cells, could make a transplant safer, even for donor-recipient pairs who aren't perfect matches.

She came to U of L in 1998 under Bucks for Brains, a state program designed to bring top researchers to Kentucky universities, and she tested her procedure on her first sickle cell patient in November 2005. The first two, including Amos, were treated at Kosair Children's Hospital.

Treatment of patients moved to Duke in North Carolina about three years ago, Ildstad said, after the NIH encouraged her team to branch out beyond Kentucky. But while Duke is a larger research institution with more clinicians available to do the work, Ildstad said she hopes to resume enrolling patients for treatment in Louisville as well in about a month.

Kurtzberg, director of Duke's pediatric blood and marrow transplant program, said her team "very much wanted to participate" and believes the procedure holds great promise.

"We wouldn't be doing it if we didn't," she said.

Researchers at Northwestern University in Chicago also plan to begin treating sickle cell patients through the study in about six months.

Russ Prough, vice dean for research at U of L's medical school, said he's excited about the collaborations, and counts Ildstad among the most high-powered medical researchers at U of L.

"Before Bucks for Brains, we had one or two people who really were doing impressive research," he said. "Bucks for Brains brought a whole critical mass of people."

'WORK A MIRACLE'

Transplant gave boy entirely different life

When Tony Igwe heard about Ildstad's study, he consulted with his wife, Eucharia. Both decided it was worth a try for their son.

The Nigerian-born couple had watched Amos suffer for years. At 3, he developed a pneumonia-like complication called acute chest syndrome that almost killed him.

As Amos grew older, he was pale and tired, hardly ate and suffered joint pain that made it difficult to get around. He needed transfusions almost monthly. He was often absent from school. The Igwes ran their lives around his illness, skipping vacations and curtailing activities for their other three children, who do not have the disease.

"You didn't know what was going to happen day to day," Eucharia said.

To get sickle cell disease, a child must inherit one gene from each parent, and parents can either have the disease or be carriers, as are the Igwes.

Doctors eventually tested everyone in the family to see if they could donate marrow to Amos. Youngest daughter Chi-Chi proved a perfect match.

"God gave me this child," Tony said of Chi-Chi, now 8. "Maybe He's trying to work a miracle."

Amos was among the 17 percent of sickle cell patients who have perfect bone-marrow matches. Some other study subjects do not, but Ildstad's technique also allows a partially matched mother, father or sibling to donate.

In the procedure, marrow cells are harvested from the donor, sent to Louisville, and processed in a clean room to remove active immune system cells and bring out the facilitating cells. Meanwhile, recipients are "conditioned" with chemotherapy and radiation, but in much lower doses than someone getting a traditional bone-marrow transplant. Such low doses are one reason the technique is safer than a traditional bone-marrow transplant.

Another reason is that the facilitating cells, and marrow processing, are thought to greatly reduce the possibility of graft-versus-host disease. Ildstad said a traditional bone marrow transplant carries a 25 percent chance of graft-versus-host and a 10 percent chance of death — a price doctors deem too high for treatment of a noncancerous condition.

But Ildstad's procedure, though safe enough to be done on an outpatient basis, is not without risks. Even low doses of radiation can carry a long-term risk of cancer, she said, and anti-rejection drugs can increase the chance of infection even if tapered after six months, and ended after a year.

Amos no longer takes anti-rejection drugs and hasn't had any problems since the transplant. Jeanne Flowers, principal at St. Albert, said his health is so much better that "he's a different child."

During a recent gym class, his sneakers squeaked as he scrambled for a basketball, grabbed it from a classmate and shot toward the basket.

"For the past four years, he's never been at the hospital overnight," his father said. "Before, he never eats. Now he eats more than anyone."

In Amos, Ildstad said, chimerism worked. About 30 percent of his marrow can now be traced to 8-year-old Chi-Chi — who said she's happy to have helped.

"He's my brother," she said. "I love him."

'HEALTHY SKEPTICISM'

Not all persuaded, but optimism exists

Amos and the other patient treated in Louisville, who has since moved out of state, were successes, but not all cases have been. While one of the others appears successful in the early stages, and another recent case is still pending, two of the transplants didn't take.

DiPersio, of Washington University, is skeptical about chimerism and predicts that researchers will have trouble recruiting enough test subjects in the long run because African Americans are often reluctant to join clinical trials. It's a legacy of the infamous Tuskegee experiment, in which black men with syphilis were left untreated.

"The question is whether we can do this on a large scale," he said. "You must have healthy skepticism when you look at these things."

Other researchers are much more optimistic.

Dr. Catherine Wu, an assistant professor of medicine at Harvard who does similar work, said Ildstad's trial fits into a growing field of modified bone-marrow transplants that other scientists are testing. This line of research, along with gene-therapy studies, represents the leading edge of the search for a lasting and widespread sickle cell cure, she said.

But Wu and others caution that it's still early in the research process. Even if all goes well, Duke's Kurtzberg said the procedure would need to go through the lengthy process of federal approval before being offered as a standard treatment.

Yet Dr. Ashok Raj, a U of L physician who treats sickle cell patients at Kosair, said research success would be a godsend for the suffering children he sees every day.

While sickle cell treatments have improved over the years, the disease remains disabling and deadly.

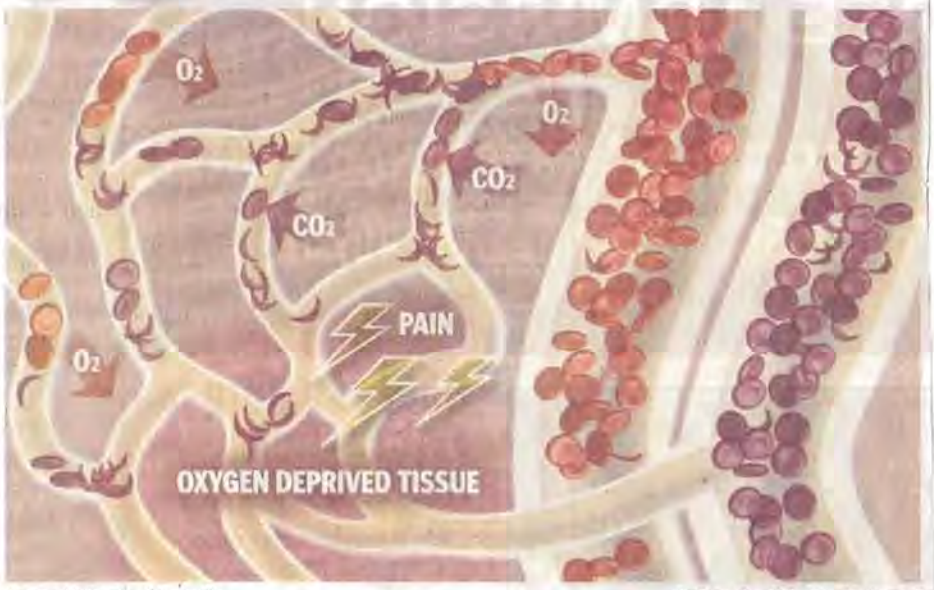
"It would be fantastic if this technology makes a big impact on our kids," he said. "That would be a very remarkable achievement."

Reporter Laura Ungar can be reached at (502) 582-7190.

The problems with sickle cells

Normal red blood cell
The shape of the normal blood cell allows it to move freely through the smallest of capillaries, delivering oxygen to organs and tissues and taking away carbon dioxide.

Sickle cell
Clumps of sickle cells block the blood vessels leading to limbs and organs. Blocked blood vessels can cause pain, infections and organ damage.



Source: University of Louisville

By Steve Reed, The Courier-Journal

SICKLE CELL DISEASE

What is it?: A disease in which the body makes sickle-shaped red blood cells instead of normal doughnut-shaped cells. Clumps of sickle cells block blood flow in the vessels leading to the limbs and organs, causing pain, infections and organ damage.

Causes: Those who have the disease inherit two recessive genes, one from each parent. Carriers without the disease are considered to have sickle cell "trait," which is thought to be protective against a deadly type of malaria. It developed in areas where malaria is endemic.

Who's at risk?: It is most common in people whose families come from areas prone to this malaria, such as Africa, South or Central America (especially Panama), the Caribbean islands, Mediterranean countries, India and Saudi Arabia. In the United States, it affects about 70,000 people, mainly African Americans.

Signs and symptoms: Commonly fatigue, shortness of breath, dizziness, headache, coldness in the hands and feet, pale skin, chest pain. Sudden pain throughout the body is also common and is called a "sickle cell crisis," which occurs when sickle blood cells form clumps in the bloodstream.

Complications: Hand-foot syndrome, which causes fever and pain and swelling in hands and feet; splenic crisis, which causes the spleen to shrink and may require blood transfusions; infections; acute chest syndrome, similar to pneumonia; pulmonary arterial hypertension, which makes it hard for the heart to pump blood through the lungs; delayed growth and puberty in children; stroke; eye problems; gallstones; ulcers on the legs; and multiple organ failure.

Diagnosis: Newborns are screened for the disease, and if the test shows a problem, a second blood test is done.

Treatment: Among others, bone marrow transplants; medicines and fluids for pain; a medicine called hydroxyurea to help prevent painful crises; blood transfusions.

Prognosis: In the past, sickle cell patients often died from organ failure between ages 20 and 40. Now some patients can live into their 50s and beyond — though half still die by 40.

Sources: National Heart, Lung and Blood Institute; National Institutes of Health; Dr. Suzanne Ildstad, University of Louisville

Family thrown a double blow of dying siblings

By Laura Ungar
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The Courier-Journal

Five years ago, Valicia Starks felt her teenage daughter's grip grow weak as she succumbed to sickle cell disease. Now she clutches the hand of her dying 23-year-old son.

He wastes away beneath crumpled covers with his belly distended and oxygen tubes snaking from his nose. Across from his bed hangs a shadow box containing dried roses from his sister's casket.

His parents and nurses expect him to die within months of the same inherited blood disease that killed his younger sister, Dominique, at 17.

Dominique Starks died of sickle cell disease in 2005.

University of Louisville scientists are working to cure the disorder, but their research comes too late for the Starks family of Shively, whose story reveals the heartbreaking toll of a disease that kills and disables African Americans by the thousands and currently affects more than 1,700 people in Kentucky and Indiana.

"We've seen all the effects of this disease twice," said Terrell's father, Carl, a computer-operations specialist with Humana. "It's a horrible disease."

Carl and Valicia, who also have an older son without sickle cell, say they try not to dwell on Terrell's inevitable fate. Instead, they spend hours each day sitting in his room, talking to him, administering medications and feeding him.

Though Terrell, who is 6-feet-1 and 130 pounds, finds it difficult to eat these days, he keeps some snacks on a shelf and especially likes the salt on Pringles potato

See **STARKS**, A9, col. 1

STARKS | Family thrown a double blow as second sibling nears his death

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chips. A drawer and refrigerator in his room are filled with medicines — he takes nearly 20, four times a day.

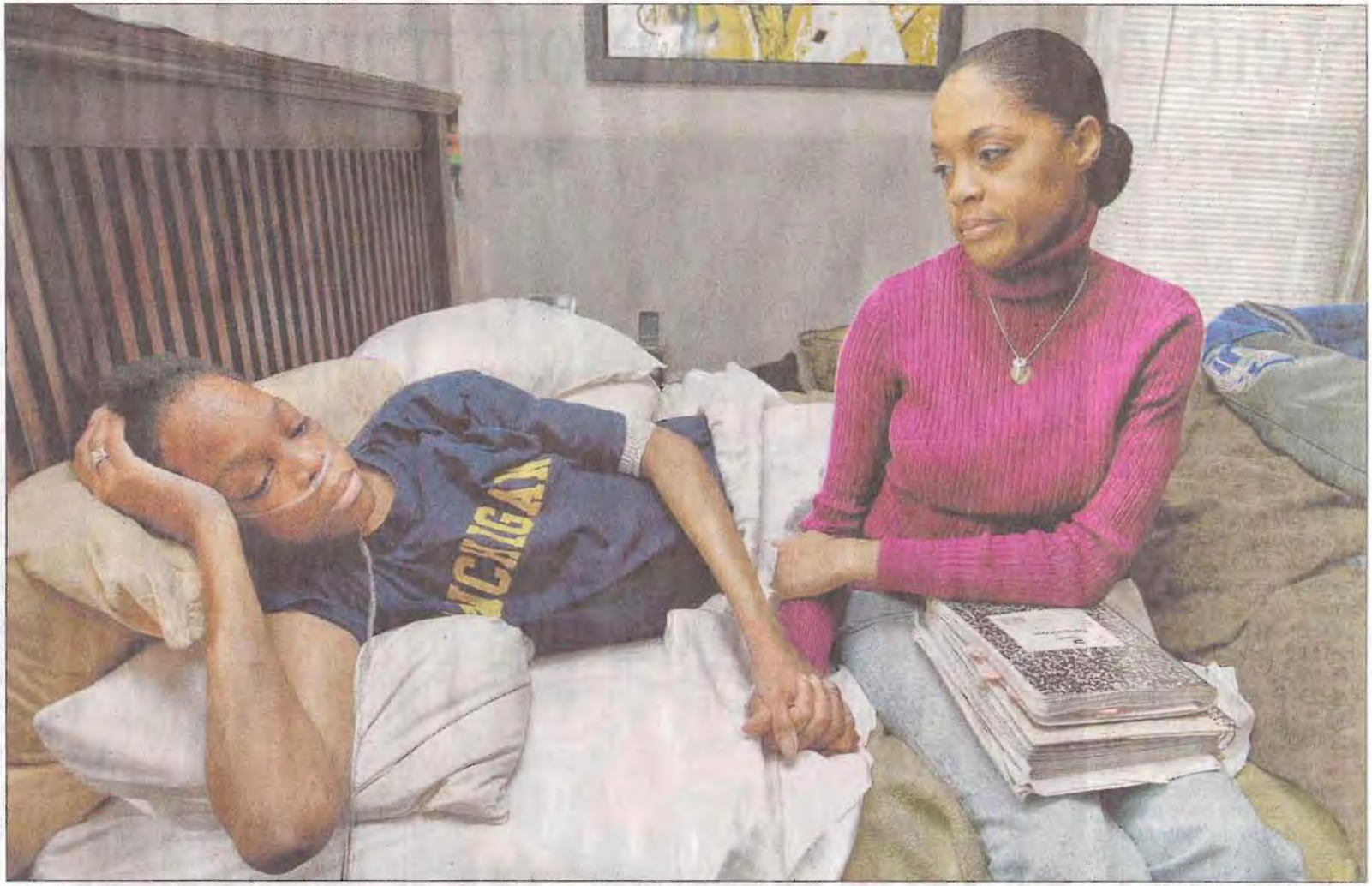
Sickle cell causes "such a tremendous amount of suffering," said Dr. Goetz Kloecker, a hematologist and oncologist at U of L's James Graham Brown Cancer Center who has treated Terrell for several years. "Now that he's on hospice, our main goal is to keep him comfortable."

Terrell tries to distract himself from his pain by coloring, watching television, playing Sims video games and snuggling with his miniature dachshund, Ozzy.

"That's all I have left to do," he said.

But he also dares to imagine what his peers are doing in the world he would be launching into if he were healthy.

"I think I would be finishing college now," Terrell said. "I think about that every single day."



By Sam Upshaw, The Courier-Journal

Valicia Starks clutches the hand of her son Terrell Starks as she sits on his bed in their Shively home. Terrell Starks, 23, has sickle cell disease and he and his family are preparing for him to die. Terrell's younger sister died from the disease in 2005.

HARROWING DECLINE

Sister's illness was a painful struggle

Born 14 months apart, Terrell and Dominique shared a genetic legacy they inherited from two parents with sickle cell "trait," who don't have the disease but carry a gene that can be passed on.

As a baby, Terrell screamed inconsolably, had a constant low-grade fever and often suffered swollen hands and feet. By the time doctors diagnosed him, Valicia was pregnant with Dominique, who was diagnosed at around 9 months.

As young children growing up in Michigan, Terrell said he and his sister were "joined at the hip."

"We did everything together. We would pick out each other's clothes, do puzzles, make dinner together," said Terrell. "People thought we was twins."

As a little girl, Dominique loved dancing and climbing trees. But when she was 12, Valicia recall ed, she turned to her mom as they watched TV after a dance recital and said, "My chest hurts."

Within two months, she suffered a massive heart attack, a stroke and congestive heart failure. She developed a fungus in her lungs that caused scarring and led to pulmonary hypertension that triggered intense pain.

Before the heart attack, doctors had suggested she get a bone-marrow transplant to stop the organ damage. But such transplants are dangerous, and she was ultimately deemed too sick.

Doctors, under judges' orders, also gave blood transfusions twice to her and once to Terrell against the wishes of their parents, who are Jehovah's Witnesses. But in both cases, Valicia said, doctors stopped the transfusions when organs began to fail.

During Dominique's teen years, she gradually lost her hearing and was left profoundly deaf. Her parents learned sign language.

One day in 2003, while Dominique slept in a hospital bed, Valicia traced her own hand and made a card for her daughter that included the words: "I am your hands. My hands will hold you up. The touch of my hands will soothe your pain. My hands will guide you, dress and feed you. I just wish my hands would heal you."

But they couldn't.

Eventually "I could not even hold my baby because the touch of my hand would give her pain. ... My own mother touch was too much," said Valicia, 45.

In March 2005, doctors gave Dominique a week to live. Valicia recalled her saying: "I'm glad they told you I was dying. I didn't have the heart to tell you. ... I don't want you to be sad when I go."

"If I could," Valicia said she told her daughter, "I would give up my heart and lungs for you."

Three days after the doctors' pronouncement, Valicia said, Dominique lay back in her mother's arms and signed, "Thank you for being my mom."

Valicia signed back: "You're welcome. I love you so much," then held Dominique's hand as she slipped away.

Living with the dying: The story of Terrell Starks

Follow Terrell Starks and his family's story online at courier-journal.com as reporter Laura Ungar and photographer Sam Upshaw Jr. document the strong ties — and the ability to live in the moment — that hold this family together even as death approaches.

Through videos, photos, blogs, social media and stories, learn how Terrell and his family treasure life one day at a time.

RELEARNING LIFE

Early difficulties, then brief reprieve

Terrell's life has in many ways mirrored his sister's.

When he was 8, doctors removed his gallbladder, and a week later his right lung collapsed.

His left lung collapsed after he was placed in a medically induced coma. Immediately afterward , he went into a regular coma and remained that way for four months.

When he woke up, he said, "I had to learn how to walk and eat all over again."

He was home-schooled until fifth grade, and then attended a half-day school for disabled children for a while.

By his freshman year, he was back in a normal school and had regained some of his health. Pain was almost constant, but he was well enough to play drums in the marching band, participate in Students Against Drunk Driving and make the honor roll.

"In high school, I was able to have a pretty decent life," said Terrell, whose blue and gray high school letter jacket still hangs in his closet. "I was happy. I realized how precious it all was."

His adolescence gave him a taste of the independence he would never achieve.

After Carl taught him to drive, Terrell got his license but never got the chance to drive alone. He landed his only job at 18, working as a part-time water-park attendant in Michigan, which he remembers as "fun while it lasted."

He never felt well enough for college, but did manage a semester of culinary training, with the goal of becoming a chef.

But in 2004, a massive heart attack, then a stroke, ended that dream.

Since then, the family has struggled with his steadily declining health and the related financial strain.

Even with three insurance plans, they pay $10,000 to $15,000 a year out of pocket for Terrell's medications and care. The family moved to Louisville three years ago for Carl's job, and Valicia recently took a job as a counter manager at Von Maur. But the Starkses still can't afford a headstone for Dominique's grave in Michigan.

In their time of need, fellow members of the Kingdom Hall of Jehovah's Witnesses call the Starkses almost daily and bring family meals once a week. A hospice nurse visits once a week. Terrell gets sleepy more often, is having trouble swallowing pills and relies on pain medication just to breathe comfortably.

Kloecker said Terrell is now in the final stage of heart failure. He has recommended transfusions that could possibly extend Terrell's life — he doesn't know for how long — but said he respects the family's religious objections and admires his patient's philosophical outlook, strong faith and sense of peace.

On Terrell's bedroom walls are reminders of his past and future.

Near his bed is a stylized photo of the family during a Disney cruise, on another wall a photocopied photo of Terrell and his sister making funny faces and pressing their heads together under the words "Wanted: Dead or Alive."

But even as the family stands on the precipice of a second death, they cling to life.

"We are happy with the moment," Valicia said. "As long as Terrell is fighting, I will fight."

Reporter Laura Ungar can be reached at (502) 582-7190.

CARE FOR ADULTS

Patients say Louisville lacks targeted programs

By Laura Ungar
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The Courier-Journal

As an adult struggling with the pain and fatigue of sickle cell disease, Le'Nata Townsend feels ill-served by Louisville's medical community.

Local doctors don't seem to truly understand sickle cell, she said, and many treat patients as simply wanting a fix of pain medication.

"Research is good, said Townsend, a 31-year-old single mother of four who travels to Cincinnati for care about every three weeks. "But what about us, those who are living with" sickle cell? "What about treatment?"

Townsend isn't alone in her dissatisfaction.

While treatment for children fighting sickle cell in the Louisville area is very good, some adult patients say their care doesn't measure up — and they would like to see a comprehensive sickle-cell center similar to the one in Cincinnati.

Experts said such sentiments may reflect national growing pains among adults with sickle cell disease — a relatively new patient population thanks to improvements in treatment such as hydroxyurea, a drug that helps prevent pain crises and decreases the need for blood transfusions. In the 1970s, victims rarely lived past 20.

Dr. Vivek Sharma, a University of Louisville hematologist and oncologist, acknowledged that care could be better for adults.

"The patients do get taken care of, and the physicians are good overall," said Sharma, who treats sickle cell patients but specializes in hemophilia and gastrointestinal cancer. But "it may not be as optimal as if there was a comprehensive program."

The University of Cincinnati has had an adult treatment program since 1985. And in 2006, the university created the Cincinnati Sickle Cell Treatment Demonstration Project, which coordinates its childhood and adult sickle cell programs, as well as primary care, community health centers and sickle cell education.

By Sam Upshaw Jr., The Courier-Journal

Le'Nata Townsend, 31, cooks an afternoon snack for son Kordell Givens, 14, at their home. She has sickle cell disease and would like the Louisville medical community to focus more of its treatment techniques on adults.

One goal is to smooth the transition from pediatric to adult care. Dr. Thomas Webb, associate professor at the University of Cincinnati, said families become accustomed to the resources of children's hospitals, which often include social workers, child life advocates and others.

"As kids," Webb said, "everything is done for them."

But expectations change when they become adults, he said, "which is difficult."

"Medical care is only part of the ball game," said Dr. Tiffiny Diers, site project coordinator in Cincinnati. As adults fighting the disease, "there's a strong need to get on with the business of living."

And that can require support. While many patients can hold jobs and raise families, they must do so while suffering pain that would put healthy people in bed, said Annette Lavender, a nurse practitioner with the project.

Townsend, the Louisville patient, said Lavender and her colleagues have a good perspective on the disease. And in addition to medical exams, intravenous pain medications and fluids, she gets counseling from the Cincinnati center.

Phillip Sanders, a 38-year-old Louisville man who also goes to the Cincinnati center, agreed with Townsend that Louisville doctors often treat sickle cell patients as drug-seekers.

That's a common problem in the profession nationally, said Dr. Imoigele P. Aisiku of The University of Texas Medical School in Houston.

Sickle cell pain is often treated with opioid painkillers, which can be addictive. And "there's a perception that 50 percent plus (of patients) are substance abuses," which isn't true, said Aisiku, who is studying the issue. "More education is definitely needed."

U of L's Sharma agreed. "What we do know is that the patients that get into a ... drug-seeking situation are in the minority," Sharma said. "That does happen, unfortunately. But they represent a small number — 5 percent."

Sharma said staff members at comprehensive centers are generally more knowledgeable about the issue and better able to hold patients accountable. But he said he doesn't know of any local doctors with the time or special interest to start such a center any time soon.

"Right now," he said, "I don't see anything happening."

Mary Medaries, Townsend's mother, said she hopes that changes.

"I'd like to get my kid back home," she said.

Reporter Laura Ungar can be reached at (502) 582-7190.

Courier-Journal, Sunday, February 21, 2010

Stem cells may stave off transplant rejection

By Laura Ungar
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The Courier-Journal

Two years ago, doctors gave Robert Waddell a choice — a kidney transplant or years of dialysis.

The 43-year-old Louisville father of four, whose kidneys were enlarged from polycystic kidney disease, chose the transplant. But he feared the possible side effects of a lifetime of anti-rejection drugs, including infection and cancer.

So he joined an experimental study that would allow him to taper off and eventually stop using those drugs.

The study, a collaboration between the University of Louisville and Northwestern University in Chicago, uses specially processed stem cells from a donor to help establish a "twin" immune system in the recipient that lets the body recognize a donated organ as its own.

Dr. Joseph Leventhal, director of the living donor renal transplant program at Northwestern, is working with U of L's Dr. Suzanne Ildstad on the study. They treated their first patient last year and ultimately hope to recruit up to 30 kidney transplant recipients.

"The results are very promising," Leventhal said. If they hold up, "it looks like this would be a safe, better approach for the large majority of people. ... It would radically transform transplants by eliminating the need for immunosuppressive drugs."

By Sam Upshaw Jr., The Courier-Journal

Robert Waddell, center, poses with his children from left, Bailey, 3; Christian, 6; Casey, 10; and Robby, 9; at their home in St. Matthews. Waddell received stem cells as part of a kidney transplant. The stem cells from a donor to help establish a "twin" immune system in the recipient.

"The results are very promising." If they hold up, "it looks like this would be a safe, better approach for the large majority of people. ... It would radically transform transplants by eliminating the need for immunosuppressive drugs."

Dr. **JOSEPH LEVENTHAL**, *Northwestern University*

To be eligible for the study, patients can have various kidney diseases, but can't have an infection such as HIV. They must also have a suitable living donor — although the person doesn't need to be perfectly matched.

Waddell's donor wasn't even a family member. He got his new right kidney from Hugh Haydon, a friend and fellow parishioner at Our Lady of Lourdes Catholic Church.

Haydon, 50, said he considered his friend's medical predicament and what it would mean to Waddell and his family if he didn't get a new kidney. Then he offered his.

"It was a privilege to do it," said Haydon, who lives in Louisville but runs Kentucky BioProcessing in Owensboro.

Haydon said the stem-cell harvest, done at Northwestern in Chicago, was the hardest part. He recalled getting a central line in an artery in his neck and being hooked to a machine for about eight hours.

His bone-marrow cells were then processed in Louisville to bring out "facilitating cells" that researchers believe help transplants succeed. In traditional organ transplants, recipients face a significant danger of graft-versus-host disease, in which cells in the transplant see the recipient as foreign.

Waddell, a finance manager at Brown-Forman, said the roughest part for him was the pre-transplant "conditioning," which included chemotherapy and radiation.

"Going through it was a lot worse than I expected," he said.

The kidney transplant, along with the transplant of Haydon's stem cells, took place at Northwestern Memorial Hospital in Chicago in May. Waddell recalled feeling great immediately afterward, then getting nauseous and losing weight as the effects of the chemo lingered.

But when those effects faded, he said. "I would just walk around and say, 'I feel good.' "

Waddell has had three-month and six-month checkups at Northwestern and is awaiting an annual checkup in the spring. He also gets monthly tests at Jewish Hospital Medical Center East, which are sent to Leventhal to see if his donor's cells are co-existing with his own.

So far, they are. He has tapered his anti-rejection drugs from two to one and hopes to soon get the go-ahead to stop them.

He said he hopes his new kidney lasts for life — something doctors aim to achieve through this procedure. Today, Leventhal said, organs last about 20 years.

"I didn't know for sure if it would work. So far, it seems to work," Waddell said. If the study is successful, "it definitely is going to be the wave of the future. Based on my results, I believe it."

Reporter Laura Ungar can be reached at (502) 582-7190.

MEDICAL INNOVATIONS

HELP FOR GENETIC METABOLIC DISORDER

Bob Evanosky said he and his wife, Sonya, were "handed three death sentences" in 2005, when all of their children were diagnosed with metachromatic leukodystrophy, a progressive and fatal genetic metabolic disorder that leads to muscle wasting, vision loss, paralysis and dementia.

But one of the Illinois couple's sons — 8-year-old John — has been offered hope through an experimental treatment pioneered by Dr. Suzanne Ildstad of the University of Louisville and Dr. Joanne Kurtzberg of Duke University. (His siblings, including a twin brother, didn't qualify for the clinical trial.)

Last year, John received a modified, safer version of a bone-marrow transplant similar to the one used to treat sickle cell disease. Bob Evanosky was the donor, and his marrow cells were sent to Louisville for processing before being given to John.

Before the procedure, John was a quadriplegic on a ventilator who could not speak. The treatment is not expected to cure him, but his family and doctors hope his condition improves slightly and that he doesn't reject the marrow.

Bob Evanosky said he is already noticing improvements and added that doctors plan to eventually wean John from anti-rejection drugs.

"We are starting to see subtle changes in John's disposition," said Evanosky, who lives outside Chicago. "There's some improvement in his (breathing). There's some movement in his body. He can move his arm and stretch. ... This probably is the most optimistic technology to come down the pike."

Evanosky family photo

Sonya and Bob Evanosky of Aurora , Ill., with their three sons, from left, John, Jack and Christopher. The boys have a fatal genetic metabolic disorder. John was eligible for an experimental treatment pioneered in part by Dr. Suzanne Ildstad of the University of Louisville.

HAND, FACE AND SIMILAR TRANSPLANTS

Today, a soldier needing a new hand to replace one lost in war would face a lifetime of anti-rejection medications. But research by Ildstad and her team could someday eliminate the need for such potentially dangerous drugs.

The research has been supported by the U.S. Department of Defense, which gave U of L's Institute for Cellular Therapeutics a $1.6 million grant last September.

Transplanting bone-marrow stem cells from the donor, along with a composite tissue transplant such as a hand transplant, is designed to create a "twin" immune system that helps the body recognize the transplanted tissue as part of itself.

If it works, researchers said the potential for transplantation without anti-rejection drugs could revolutionize reconstructive surgery.

MULTIPLE SCLEROSIS AND OTHER DISORDERS

U of L researchers believe safer bone-marrow transplants could also treat relapsing-remitting multiple sclerosis and a host of other autoimmune disorders.

In diseases such as MS, rheumatoid arthritis and lupus, the body's immune system mistakenly attacks its own organs, tissues and cells. Some diseases attack specific organs, while others attack several organs. Researchers believe bone-marrow transplants could halt the progression of such diseases.

Currently, however, bone-marrow transplants can be dangerous. A common and potentially fatal complication is graft-versus-host disease, in which the cells in the donor marrow attack the recipient's body. Also, bone marrow or stem-cell transplants require donors and recipients to be a perfect genetic match.

But researchers are working on a less toxic "mini" bone-marrow transplant, which doesn't require a perfect match and may be performed on an outpatient basis. One clinical trial treats MS through a bone-marrow transplant with stem cells and "facilitating cells," which help the donor cells to "take."

SICKLE CELL RESEARCH AT UK

Dr. Robert Means, an internal medicine professor at the University of Kentucky, also is studying sickle cell disease, focusing on a growth factor called PlGF, which regulates blood-vessel development.

It is associated with inflammation, and is markedly increased in the bone marrow of sickle cell patients. Means, whose research so far is limited to laboratory cultures, said he wants to better understand the inflammation process and the role it may play in sickle cell disease.