

Three Times Is a Charm

BY RUTH ANN HENSLEY



Whether it is in the form of miraculous signs, lofty wishes or four-legged creatures, three-time cancer survivor Sierra Josephsen is living proof that the adage is true.

It was an autumn afternoon in a suburban Illinois supermarket, and 5-year-old Sierra Josephsen was down to her last dollar. Some might say she had fallen on hard times, and in many ways they would have been right. But Sierra's concerns went much deeper than mere finances. That day, the vibrant girl sporting a bob of golden hair and shimmering hazel eyes was consumed with only one thought—to win; to beat the odds of the game she was playing.

While her mother scanned the aisles for groceries, Sierra tentatively put her last bill in the crane machine. With a firm grip on the handle, she slowly lowered the metal jaws to clench a prize from the stack of stuffed animals filling the glass box.

Passersby paid the girl little notice. They couldn't possibly know that Sierra had recently received her third cancer diagnosis...that a doctor had told her parents, "You will be burying your child" and that the family was anxiously awaiting a phone call from a hospital that offered their last hope.

Suddenly, Sierra felt a tug at the end of the chain. With a resounding thud, the crane released its treasure into the collection bin. "I won!" she breathlessly exclaimed, clinging to a small doll wearing a "Miracles Happen" T-shirt.

It was the first sign that perhaps Sierra could beat the odds in a game that really mattered, where the stakes were life and death.

Survivor

"We come to St. Jude with that doll every time," Sierra's mom, Sandy, says, "because miracles do happen."

Ed and Sandy Josephsen witnessed a miracle the day Sierra and her identical twin sister, Savana, were born. "I was so happy that they were healthy," Sandy says.

The girls pursued the inquisitive, playful and boisterous activities that all toddlers enjoy, but when they turned 3½ years old, Sandy noticed some disturbing changes in Sierra. "She would cough until she turned white," Sandy recalls, "and her tummy started getting bigger."

Sierra's pediatrician concluded that she had asthma and prescribed daily breathing treatments. After numerous



“You’ve got to have hope,” says Sierra Josephsen. The three-time cancer survivor should know. Doctors at another institution instructed Sierra’s parents to make funeral arrangements for their daughter. Then the family found St. Jude, which had just begun a trial using the drug topotecan for patients with Wilms tumor. “Some people say, ‘Three strikes, you’re out,’ but not at St. Jude,” says Sierra’s mom. “Three times is a charm.”

breathing treatments, Sierra’s stomach was still distended. “Finally,” Sandy recalls, “I said to Sierra’s doctor, ‘Her tummy does not look like Savana’s at all.’” The doctor intently pressed on Sierra’s abdomen, and the color drained from his face. “Let’s go down the hall for a chest X-ray and an ultrasound—and call your husband,” he said.

Sandy called her sister first because she lived nearby. “Sue, you’d better get over here. I think they’re going to tell me that Sierra has pneumonia,” Sandy said. Moments later, the family learned that Sierra had cancer. “I had to leave the room,” Sandy says. “I couldn’t breathe.”

Sierra was found to have Wilms tumor, also known as nephroblastoma.

The fourth most common type of cancer in children, Wilms tumor arises from the disordered development of embryonic kidney cells—immature cells that normally regress by birth but can become cancerous if they persist into childhood.

Two days later, surgeons removed a 16-centimeter tumor and Sierra’s right kidney. It was a frightening blur of activity for the Josephsen family, but after the successful surgery they could breathe again. “Sierra was a stage II, which meant there was a 90 percent chance she would never have cancer again,” Sandy says, “and they told us they got the whole thing.”

Sierra won her personal version of *Survivor* and a wish to go to Walt Disney

World®. No one imagined that during a regular check-up, 14 months later, doctors would announce that her cancer had returned.

“I felt like I was shot in my chair,” says Sandy, who remembers every moment of that day with *Rain Man*-like adeptness. “It was September 11, 2002,” Sandy says. “Bad date.”

Sierra’s cancer had returned in exactly the same place as before, but the tumor was large and the prognosis was not good. After high-dose chemotherapy reduced the mass to the size of a tennis ball, surgeons removed it.

“They said they got the whole thing,” Sandy recalls. “We followed up the surgery with a double stem cell trans-

plant and radiation, and I was thinking, 'Okay, this time we beat it.'"

After enduring a recurrence of cancer, five bowel obstructions and her third major surgery, Sierra won round two of a deadly competition and a wish for a dog — a black Labrador retriever named Survivor. Why Survivor? "Because that's what I am!" Sierra proclaims.

Topotecan

Only eight months after Sierra completed radiation, doctors instructed the Josephsen family to make funeral arrangements. The girl's cancer had returned for a third time. "You know it's bad when the oncologist is crying with you," Sandy says.

Wilms tumor, which has an 85 percent survival rate, proved a wily adversary for Sierra, but she was about to enlist a powerful ally.

"I told the oncologist, 'We can't stay here any more; you're not giving

us any hope,'" Sandy says. "When the doctor asked where we would go, I said, 'Anywhere—anywhere that gives us hope.'"

Sierra's pediatrician conducted a frantic search and discovered that St. Jude Children's Research Hospital had just begun a trial for Wilms tumor patients using the drug topotecan.

"It was a godsend that they were running the trial at the same time for the same type of cancer that Sierra had," Sandy says, reliving the joy of that discovery. "It was another sign."

Laboratory studies directed by Jeffrey Dome, MD, of Hematology-Oncology and Peter Houghton, PhD, of Molecular Pharmacology showed that topotecan was an effective drug in the treatment of Wilms tumor. "We also had encouraging data from patients treated on Phase I studies of topotecan, conducted at St. Jude," Dome says. "The combination of the laboratory data and early clinical data turned on the light bulb to start a clinical trial of topotecan specifically for patients with Wilms tumor."

Once team members determine the medication's most effective administration schedule, they adjust or individualize the topotecan dosage as part of a treatment regimen called pharmacokinetic targeting. "It's beautiful in a way because we measure the topotecan levels in the blood, and it's variable from person to person; so if the dose is too low we increase it and vice versa," Dome explains. "There are very few chemotherapy drugs where we can do that, so it's a tremendous benefit."

Dome says the promising results of this study, unique to St. Jude, have prompted the Children's Oncology Group and the International Society of Pediatric Oncology to consider a proposal using topotecan as the standard chemotherapy for recurrent Wilms tumor.

Hope

As a result of this treatment, 8-year-old Sierra has been cancer free for nearly two years. "Being a three-



"I can never say how thankful I am to Dr. Dome, the PK [pharmacokinetic] nurses and everyone who has helped us on our journey here," Sandy Josephsen says. "How do you repay a hospital for saving your child's life?"

time survivor of Wilms tumor is extremely rare because survival rates diminish with each recurrence," Dome says. "The further out she gets, the better off she is."

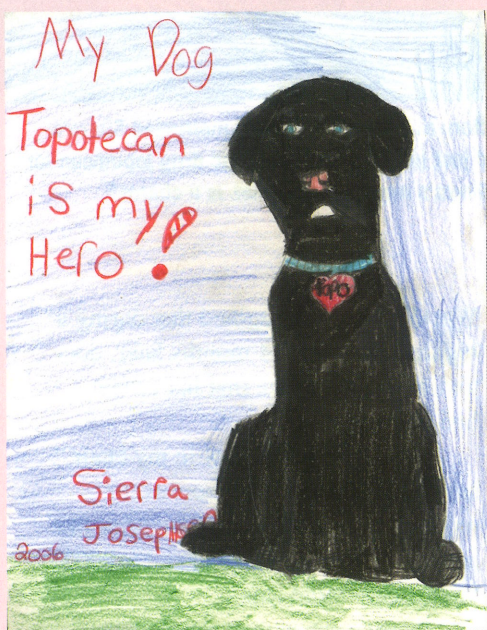
"She knows exactly what it means to never give up," says Lisa Walters, RN, one of the pharmacokinetic nurses who cared for Sierra. "She will undoubtedly continue to be an inspiration to others, to give them hope."

Sierra, who says she gets her strength from her sister, Savana, had beat down her fierce competitor for the third time. So what could she possibly wish for after that? "Another dog," Sandy says with a roll of her eyes. "She wanted another black Lab, and she wanted to name him Topotecan." Why Topotecan? "Because Topotecan saved my life," Sierra says matter-of-factly.

Sierra received the dog she calls "Topo," and her family received another sign that miracles happen.

"Some people say, 'Three strikes, you're out,' but not at St. Jude," Sandy says. "Three times is a charm."

Perhaps that's why Sierra is wishing for a third black Labrador these days. She's even picked out the name—Hope. Because, as the young cancer survivor explains, "You've got to have hope." ●



Sierra named one of her dogs Topotecan, after the drug used to eradicate her tumor. She gave a photo of the canine to Clinton Stewart, PharmD, of Pharmaceutical Sciences, who contributed to the Wilms tumor protocol. "When people tour my lab, I tell them how much things cost," Stewart says. "One instrument is \$80,000; one is \$400,000. But then I tell visitors, 'This is what makes it all worthwhile; this is priceless'—and I pull out a picture of Topotecan."