

Conor's Story

On the morning of July 18, 2005, Conor, fifteen months old, woke up and just wasn't right from the get-go. I naturally assumed that he was in pain from several baby teeth that were erupting all at once, so I gave him some Children's Tylenol and carried on with our normal routine. Later in the day his daycare called me at work. "Conor just hasn't been him self and doesn't seem well," they said. So, I quickly gathered up some work to finish later and picked him up. Although obviously in a little distress, it didn't seem anything out of the ordinary for a teething child.

During the night, Conor developed a temperature of 103°F and an unusual cough, symptoms obviously not associated with teething. The previous week, the daycare had posted a notice that a child there was diagnosed with roseola, including the common symptoms associated with the virus such as an unexplained high fever. However, Conor's cough sounded more characteristic of pneumonia. After a disturbed night, we decided to take him to the pediatrician for the cough. Conor's doctor also noticed that the cough did sound more like pneumonia, but unlike pneumonia, Conor's lungs sounded clear. The pediatrician ordered a chest x-ray to rule out any form of pneumonia.

While we were waiting in the examining room with the door open, I noticed that the doctor briskly left his office and then returned to see us shortly afterwards with a very concerned look on his face. He told me the radiologist had identified a large mass in Conor's chest. To avoid discussing more in front of Conor's older sister, he took me into his office and showed me the x-ray on his computer screen. The mass went from right side of his chest and crossed the midline. I called my husband, Nick, and told him that he needed to come to pediatrician's office immediately, as I knew exactly what this meant. Meanwhile, arrangements were being made to admit Conor to the Rady Children's Hospital.

Later that afternoon, once Conor's initial blood work and CAT scans results were back, the attending pediatrician and our nurse at Children's Hospital took us into a private room. Nick was holding Conor in his arms as the doctor told us that it was very likely that the mass in his chest was neuroblastoma. The mass was extremely large and had begun pushing against Conor's trachea, resulting in the unusual cough. Since both Nick and I work in the field of cancer biology, we knew it was the worst possible news.

Over the next several days in the critical care unit, Conor had additional blood work, full body x-rays, bone scans, MRIs, a tumor biopsy and a portal catheter implanted. As the results trickled in, we met with the oncologist, the surgeon, the social worker, the staff psychologist, the parent liaison and the hospital administrator - a host of concerned professionals ready to watch us fall apart. As we waited for the pathology reports to come back, Conor was transferred to the oncology ward. Until then, we had been too caught up in the urgency to figure out how invasive the cancer was. The minute we went to the oncology ward, reality

set in and left us reeling. It was an extremely quiet, sober place, very different from the critical care unit. We were faced with the fact that our child really did have cancer. This wasn't just a nightmare, it was our lives and we really were living it.

Over the next ten days, we waited for reports from several pathologists all over the country who analyzed Conor's biopsy material. Since the tumor did not have all of the defining characteristics of neuroblastoma, obtaining a consensus among the pathologists was not as straightforward as we had hoped or even expected. Finally, once an agreement was reached that the tumor was to be classified as unfavorable, high-risk neuroblastoma, Conor's oncologist presented us with the treatment options, although options suggests we had some choice. We didn't and neither did Conor.

As parents, Nick and I never imagined that we would be making decisions that would directly affect Conor's immediate survival. Surgery was not an option. The tumor had surrounded vital organs in his chest and the main vein, the vena cava, which delivers blood to his heart. The risk of accidentally nicking the vein during surgery and Conor not surviving the operation was a certainty. The only hope was that the tumor would respond to chemical treatment. However, Conor's oncologist warned us that due to size and maturity of his tumor, there was a very real possibility the tumor would either continue to grow or at best remain the same size.

The standard treatment options of neuroblastoma to date includes surgery, radiation therapy, chemotherapy followed by surgery and/or radiation therapy, or high dose chemotherapy followed by surgery and a stem cell transplant chased with a six month course of 13-cis retinoic acid. Surgery and radiation therapy was not an option for Conor because of the location and size of his tumor. Conor's only hope was chemotherapy and we had to choose the dosage for him (standard, high-dose, or high dose preconditioning for stem cell transplant). Conor's oncologist recommended preconditioning him for the stem cell transplant. As Nick and I reviewed the treatment protocol and the severity of adverse effects for the preconditioning (death, opportunistic infections, hemorrhaging, organ failure, guaranteed hearing loss, etc.) in addition to months upon months of hospitalization, we couldn't bring ourselves to put Conor through it. Personally, we wanted to preserve as much as we could of an acceptable level of quality of life for him, even if it was short-lived. After many agonizing hours, Nick and I took Conor's life in our hands and decided against the preconditioning and to commence with the high-dose, combinatorial therapy. On August 2nd, 2005 he began his treatment. He received back-to-back doses of carboplatin, etoposide, cyclophosphamide and doxorubicin.

The first round was easy with no immediate side effects. Two-weeks later, he began to lose his hair. Conor had not even had his first haircut yet. Before losing it all, I managed to clip off a few of his remaining platinum blond curls for his keepsake box. The following rounds became increasing difficult as his immune

system became severely compromised. After the third round and eight weeks later, he had his first MRI since being diagnosed. The tumor responded. It had shrank 40% and away from his heart and vena cava. On October 28th, Conor underwent six hours of surgery to remove the tumor from his chest and spine. He recovered quickly and did not show any evidence of paralysis resulting from the surgery. Three weeks later, he continued his high-dose chemotherapy for an additional four rounds. The last few treatments were extremely difficult as his immune system was taking longer to bounce back and his hemoglobin levels began to plummet to life-threatening levels. To keep him on schedule, he received blood transfusions in between rounds and we administered G-CSF (granulocyte colony stimulating factor) injections daily. After completing his seventh round in February of 2006, Conor had his end of treatment evaluation. He was restaged as NED (no evidence of disease), a true miracle. As an added bonus, the treatment did not cause apparent hearing loss or detectable damage to his heart and kidneys.

By Conor's second birthday at the end of March, he began to show signs of a full recovery: his hair began to grow back, energy levels returned to normal, his immune system slowly built back up and stabilized and he no longer needed blood transfusions. A relatively "normal" life gradually returned. However, Nick and I found post-treatment to be extremely difficult. During Conor's chemotherapy, we were actively doing something, but now we had to "wait and see" if the cancer would return. We were aware that the possibility was quite high that it would.

In studying the recent literature, we came across a study that compared three-year survival rates of children with high-risk neuroblastoma who received 13-cis retinoic acid therapy following chemotherapy with those who received both the chemotherapy and the stem cell transplant. According to this study, the 13-cis retinoic acid had an obvious benefit for those children that had undergone the transplant and only a modest effect on the survival rates of children, like Conor, who received only the chemotherapy. Nick and I wondered if Conor would benefit from the 13-cis retinoic acid therapy and if the benefits would outweigh the risks. The use of high levels of retinoic acid in very young children is a recent development, so the long-term side effects are unknown. In previous published studies, the concentration of 13-cis retinoic acid being administered in children was shown to terminally differentiate nearly 50% of the neuroblastoma cell lines tested. Our concern was that if high levels of retinoic acid were forcing neuroblastoma cells to terminally differentiate, then to what extent would normal stem cells be forced to terminally differentiate prematurely and how would this affect Conor's overall development (mental and physical)? Additionally, there was no way to determine if Conor's remaining neuroblastoma cells (if any) would even respond to the retinoic acid. After several weeks of consulting with world-renowned academic scientists and leading clinicians on the possible long-term side effects of the 13-cis retinoic acid on young children, the consensus was that no one knew or could even predict what the potential long-term side effects would be. In the end, we decided and Conor's oncologist agreed to start Conor on

Accutane (13-cis retinoic acid) at ten times the normal adult dose for severe acne. The treatment lasted for six months, two weeks on and two weeks off. Conor experienced all of the common short-term side effects: headaches, severe mood swings, extremely delicate sensitive skin, and hair loss. Ultimately, we will never know if we made the right decision. If Conor doesn't relapse, was it because the chemotherapy and surgery was 100% effective or did the 13-cis retinoic acid terminally differentiate any remaining cancer cells? And if the chemotherapy and surgery was 100% effective, what additional harm or long-term side effects are we responsible for?

November 2007 marked the one-year anniversary of when Conor ended his treatment. To date, he hasn't developed any notable hearing loss, mental and physical disabilities, or decrease in vital organ function. Conor continues to have MRIs every two months and we continue to "wait and see".

After Conor completed his chemotherapy, I began to investigate other pediatric cancers and their treatments. I realized that most pediatric cancers are being treated with the same chemotherapy drugs that have been around for many, many years. The only difference between now and then is that the regimens have become more intense and their success in increasing survival has plateaued at the expense of inducing severe long-term side effects. Unfortunately, very few new chemical agents are currently in development for childhood cancers simply because the market size is too small to warrant spending millions of dollars for development and clinical trials.

I began to envision a partnership between academics and industry that would tie together current scientific knowledge and technologies to design new drugs and develop innovative approaches for treating pediatric cancers. After discussing these ideas with a fellow colleague, Dr. Martin Latterich, who has extensive experience in academics, industry and personalized medicine, we began to envision such a partnership in the form of a clinical research institute. This institute dedicated to pediatric cancer research would perform translational studies and molecularly guide the therapies to reduce the severity of side-effects from the treatments and provide a better quality of life for our children who have gone through so much. It would offer them better options for the present and opportunities for a healthy future.

-Beth Anne Baber, Ph.D. and M.B.A.
Conor's Mom, Co-founder and Chief Executive Officer
The Nicholas Conor Institute for Pediatric Cancer Research

"I have had dreams and I have had nightmares, but I have conquered my nightmares because of my dreams." -Jonas Salk