

Hope in hopeless causes



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Dr. Bruton took one more careful look at the boy who lay immobile on the exam bed before glancing back at his notes. “You are an interesting case, Joseph.” “Although it’s hard to tell the exact underlying reason for your recurrent bouts with pneumonia, the test results have come back and I think I may have an

explanation for why you are sick all the time.”

Eager to hear Dr. Bruton’s answer, Joseph’s father and mother leaned forward in their chairs.

“I believe that your son has a condition which prevents his body from producing antibodies to fight against infection. Joseph’s repeated hospitalization due to the same disease suggests that he could not develop an adequate defense to fight against it a second time, whereas normal children his age are able to do so. Additionally, I’ve tried to elicit an immune response from Joseph via typhoid and pneumococcus vaccines earlier, but he produced no response.”

“I’m not entirely sure I understand. What will this mean for Joseph?” asked his mother.

“Joseph’s body has a severely weakened immune system that makes him prone to getting very common infections, such as pneumonia,” Dr. Bruton replied.

“I am not sure if this is an acquired condition or a congenital one, but if what I believe is true, I am willing to try an experimental treatment that may help him.”

“What is that? Anything is better than letting him continue to be sick like this,” Joseph’s father inquired.

“It may sound unconventional, but if we can deliver outside antibodies via injection into Joseph’s body, which is the very thing he lacks, he might be able to fight off many of these common infections,” said Dr. Bruton. He let the family think in silence, allowing them to digest the information at their own pace.

“If that’s the only chance we have, then we must take it,” stated Joseph’s father. Dr. Bruton nodded and shifted his glance to Joseph’s

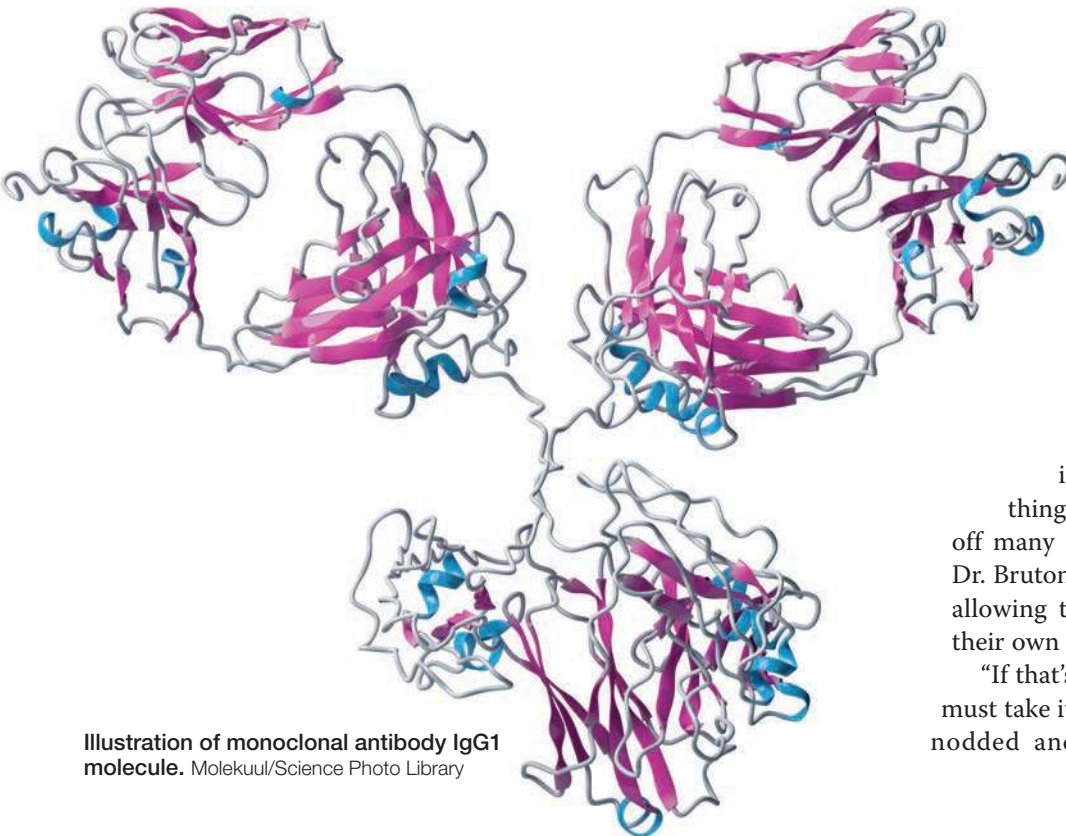


Illustration of monoclonal antibody IgG1 molecule. Molekuul/Science Photo Library



Ogden C. Bruton, MD (1908–2003).

mother, who affirmed with obvious uncertainty.

Dr. Ogden C. Bruton, an accomplished military physician, had just returned to Walter Reed Clinic in Washington D.C., for the second time after a brief tour to Europe during World War II. He was commissioned to help develop the Army's first pediatric training program.¹ As Chief of Pediatric Ward 17, one of his main focuses was deciphering the mystery surrounding an eight-year-old boy, Joseph Holtoner Jr., who came in with recurrent pneumonia infections over the course of five years. Bruton's longitudinal observations of Joseph led him to postulate that the boy had a rare case of an immune deficiency, specifically an agammaglobulinemia, of which "he is no longer able to synthesize and/or hold antibody to a specific organism."²

In a seminal publication in 1952, Bruton detailed his observations of Joseph and outlined a treatment regimen for this disorder by administering intramuscular injections of IgG, one of the main antibodies missing in Joseph's body. To everyone's surprise, results were seen almost immediately. Joseph quickly recovered, and "following the administration of human globulin at monthly intervals, he has been free of pneumococcal sepsis for more than a year..."²

From a series of critical observations, Bruton had completely shifted the trajectory of Joseph's life, one previously ravaged by "clinical sepsis at least 19 times in the previous four years," back to a normal, healthy one.

A prayer answered and paid forward

Just as Bruton was completing his work with agammaglobulinemia in the early 1950s, comedian and actor Danny Thomas was beginning to enjoy the fruits of his

breakthrough television sitcom *Make Room for Daddy*. Critics and audiences raved over his televised witty banter and comedic conversations with renowned actress Jean Hagen and then child actress Angela Cartwright. Due to Thomas' natural charm and aura, it was hard to imagine his tumultuous path to stardom.

One of nine children born to devout Catholic Lebanese immigrants in Deerfield, Michigan, in 1912, Thomas discovered his passion for acting and entertainment early on during his childhood. By the age of 10, Thomas was selling candy outside the Empire Burlesque Theater in Toledo, Ohio,³ and by 19, he had a regular Detroit amateur radio show. It was there where he would meet singer and future wife, Rose Marie. Firmly set on his passion for entertainment and pursuit of the American Dream, Thomas sought to captivate an audience of millions.

For more than two decades and throughout the Great Depression, Thomas had barely scraped by a meager living as a starving artist in Detroit. With a pregnant wife, Thomas felt financially cornered. A week before his first child was due, he had just \$7 to his name. In despair, he went to church and gave all of his money as an offering. Thomas knelt before St. Jude Thaddeus, the patron saint of hopeless causes, and prayed for St. Jude to show him the way.

The next day, Thomas received a call about performing in a Maytag washing machine sales skit at a convention that paid 10 times more than his original church offering. A few days later, his first daughter, Marlo, was born, and Thomas paid the hospital bill in cash.

The Thomas family continued to struggle, however, and Thomas continued to pray to St. Jude, "Help me to find my way in life, and I will build you a shrine."³

Eventually, Thomas' career began to make a turn for the better. His comedic talent was recognized by major agencies, leading to his move to Hollywood to begin filming his breakthrough sit-com *Make Room for Daddy* (later called *The Danny Thomas Show*). The show lasted for 12 years, and turned Thomas into a household name.

Throughout his successes, Thomas never forgot his promise to St. Jude. As he spoke with his friend and mentor, Cardinal Samuel Stritch, about what concrete form his vow would take, a plan slowly began to emerge. Thomas felt that instead of a solitary monument, the shrine would be a children's hospital located somewhere in the south. At the behest of Cardinal Stritch, Memphis, Tennessee was chosen for the hospital's location due to its social and economic struggles at the time.⁴ Finally, the hospital needed to embody Thomas' dream that "no child should die in the

dawn of life,”⁵ so it was decided that St. Jude's would be a unique research hospital devoted to curing debilitating diseases in children.

Establishing a new hospital would be one of Thomas' greatest challenges. To help fund the immense cost of building and operating the hospital, Thomas' and his wife traveled around the country in the early 1950s to garner support for his dream. Additionally, he turned to the Lebanese community for support and formed the American Lebanese Syrian Associated Charities (ALSAC) in 1957, whose main function was to raise funds for the hospital.⁴ Using his name and story to touch the heart of countless Americans across the country, Thomas was able to raise sufficient funds for the hospital and broke ground in 1958.

In 1962, St. Jude Children's Research Hospital officially opened its doors to the public. Unveiled at the front of the entrance stood a marble statue of St. Jude Thaddeus, dedicated by Thomas to fulfill his promise to the patron saint 25 years prior.

Healthy again!

I squirmed in my seat. “Mom, I don't want to watch.”

This was the third time in the same day that the nurse had tried to draw blood. I shuddered at the sound of the nurse tearing open the iodine swab packet. My skin burned to the touch of the swab as she brushed circles around my skin, as if drawing a small bullseye target marking where to thrust the needle. In silent protest, my veins slipped deep within my arm, hoping to hide behind the superficial layers of skin and fat. I looked around for distractions, but the white plastered walls of the grim pediatric ward offered no respite.

“I'm sorry Ethan, please be strong,” my mom said. Although her voice did not waver, her distressed look revealed her suppressed anxiety. The disheveled hair and wrinkles around her eyes told the story of the many sleepless nights in the hospital with her sick child. Empty apple juice cartons and unfinished meals lined the tray table beside the bed. On the other side of the exam room, my father paced back and forth nervously, having just got off the phone with my kindergarten teacher explaining my prolonged absence from class.

It was hard to remember how this specific illness began. Did it first start with an innocuous cough? Was there nasal congestion? Or was it far more insidious, beginning with a thick mucus slowly collecting in the back of my throat, preventing me first from swallowing and then breathing? Four trips to urgent care, two physician changes, and

countless restless nights within two months left my immigrant parents frustrated, broke, and without answers.

According to my reported medical record, it was first pneumonia, then it was croup, and now a mysterious disease with an unknown cause. A new illness came knocking at the door every month. Day after day, month after month, I watched the fall foliage and colorful trees outside the hospital window begin to wither away as the cold of winter approached.

After multiple rounds of blood tests, my doctor was able to tease out an anomaly in my results and implored my family to meet with a small team of researchers at St. Jude Children's Research Hospital who had taken an interest in my case. My parents, whose financial resources had dried up, were very hesitant to take on additional medical bills. However, after hearing that St. Jude's would generously cover all of the costs, my parents decided that it would be the last chance they had to seek help for me. In the blistering cold of December before the turn of the new millennia, we bundled up and drove to Memphis to meet my new health care team.

The very first thing I noticed as we pulled up to the front of the hospital was a glistening, tall white statue holding a coin and a staff. This towering obelisk was unlike anything I had ever seen. At the base of the statue were multiple rows of mysterious engravings that resembled hieroglyphics meticulously etched into the marble cornerstone. I pointed to ask my parents what it meant, however, my parents hurriedly guided me past the monument and to the main entrance of the hospital.

We were greeted by a Vanessa, a nurse practitioner, who asked us to follow her to the South Lobby and into an exam room. After a couple moments of getting settled in, there was a gentle rapping on the door. A woman with curly light brown hair highlighted with strands of gray emerged and was followed by a line of people in white coats carrying notebooks.

“Nice to meet you Ethan,” she said softly. “My name is Dr. Conley and this is my team who will be helping me take care of you.” She pulled over a chair and sat down to make eye contact with me. “We've heard a lot about you and think that we might be able to help you get better.”

Over the next two hours, Dr. Conley explained to me and my parents that there were a lot of things that were happening in my body and that it would take time to understand. “We believe that your son has a condition called X-Linked Agammaglobulinemia,” she stated. Dazed by the syllabic expanse of the word, my mom asked for it to be broken down into separate parts for

better comprehension. Using drawings and diagrams, Dr. Conley communicated that my body was missing part of its immune system and was not able to produce antibodies to fight against infection, which explained my constant illness and trips to the hospital.

“Although your son’s condition is genetic and there is no current cure, there is an effective treatment that we believe will make him healthy again,” she said. “We usually put patients with this condition on a monthly intravenous infusion of antibodies called IVIG, which will help protect Ethan from infection. We have tracked many patients with this condition and after being treated with IVIG, patients can lead a normal and healthy life.” Sensing that I was overwhelmed by all of the technical jargon, Dr. Conley turned to me, “Ethan, you don’t need to worry about a thing. We will help you get healthy again.”

Healthy! I would be healthy! Unable to contain my joy, I leapt off the exam table and started running around the room, giving everyone in the room the biggest hugs I could muster. Next to me, my parents wept tears of relief and joy, having finally found the answer to their prayers. For my parents, this meant clarity, no more sleepless nights and unending hospital visits. For me, I finally had hope for a real, normal life. Celebrations continued for a while and it took quite some time for the room to regain composure so that Dr. Conley could once again speak:

You are a very special child Ethan. One might even call you one in a million. Although you will be getting treatment back at home, we do want you to visit us every six months, just to see how you are doing.

Later in the afternoon when while my parents spoke with Vanessa in the main lobby to schedule future visits, I peered through the large glass windows and once again gazed at the tall statue outside. Figuring that this was going to be my chance, I tugged on Vanessa’s coat and asked her about the statue. She smiled and explained, “That is a statue of St. Jude Thaddeus, the patron saint of hopeless causes. It was donated by the hospital’s founder, Danny Thomas, when the hospital was built. For us, it stands as



Danny Thomas and Clergy at St. Jude's Hospital groundbreaking ceremony, 1958.

Bettmann/Contributor

a beacon of hope for those in need. If you or your family ever need anything, we will be here to help.”

I couldn’t hold back a huge smile. For the first time in a long time, things were going to be okay.

A beacon of hope

Some nights before I sleep, my restless mind drifts away and reflects on my place within the long and winding narrative of medicine. In an effort to understand more about myself and the world around me, I delved into the sciences at a young age. The more I researched my condition, the more I became fascinated with the human experience captured in past literature and the rich history that provided the foundational context to my own story.

Although Bruton had not completely solved the etiology of this enigmatic disease, his landmark discovery guided the understanding of what was later known as X-Linked Agammaglobulinemia (XLA), a rare immunodeficiency with a frequency of 1/379,000.⁶ This first known immunodeficiency is characterized by a mutation of a single gene on the X chromosome coding for an enzyme known as Bruton’s tyrosine kinase, or Btk.⁷ Btk is critical in the development of mature B cells, and ultimately the production of antibodies involved in the humoral immune response. Because of this defective genetic mutation, patients with XLA lack antibodies and are prone to develop serious and

even fatal infections if left untreated.⁸ There is no known cure for this condition; however, with continuous infusions of exogenous antibodies as first presented by Bruton, patients with this rare condition are granted passive immunity and can live a normal, healthy life.

Before the 1950s, it was presumed that infections were due to excessive exposure to pathogens or to changing properties of the body.⁹ Bruton's pioneering classification of the first human host defect over half a century ago set the stage for an exponential increase in information about the functions of the various components of the immune system. To date, more than 70 primary immunodeficiency disorders have been recognized, and these characterizations have had a profound effect on the health care of children.⁹

Since St. Jude's founding, the hospital has taken in more than 100,000 children from around the world. In 1966, a group of St. Jude patients were the first acute lymphoblastic leukemia patients to ever be successfully taken off therapy. Continuous collaboration between physicians and scientists have helped push the overall survival rate of childhood cancers from less than 20 percent when the hospital opened, to 80 percent today.⁴ While the main focus has been on pediatric cancers, generous funding has aided the study of additional rare diseases found in children.

From what originated as a personal plea for help, Thomas' steadfast promise has provided an international beacon of hope for children and families all around the world. A place where they are cared for regardless of race, religion, or ability to pay. A hospital where no suffering child is turned away.¹⁰

In an odd twist of time and space, three lives of people who would have never gotten the chance to meet have become intricately intertwined in the fabric of medicine. To this day, I wonder what the result would be if the pages of history were written some other way. Where would our understanding of immunodeficiencies stand if Dr. Bruton never made his thorough observations of a child with similar symptoms to mine? What if Danny Thomas never decided to go into entertainment, or never had the grand dream to pay his fortune forward? What would happen to me if my parents had not immigrated to the United States, or if St. Jude's never entered my life?

These are some troubling questions that could lead to an infinite string of answers, providing a countless number of possibilities and narratives. But in this very moment, it does not matter.

The narratives of Dr. Bruton and Danny Thomas are real and alive within me. The genius and tenacity that drove their works literally saved my life, and have become the mechanism for how I can live my life, but their heart

for others have given me the why. With tales of hardship, sacrifice, and selflessness as foundational fibers to inform my past, I look toward my future in medicine with renewed vigor and curiosity. Neither Bruton nor Thomas, nor anyone else for that matter, could have foretold this mysterious intertwining of fates to produce such good in this world. Likewise, I don't know where exactly my journey in medicine will lead me or the type of physician I will be, but the sheer chance and opportunity to touch the lives of others in unpredictable ways are more than enough for me to keep going.

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