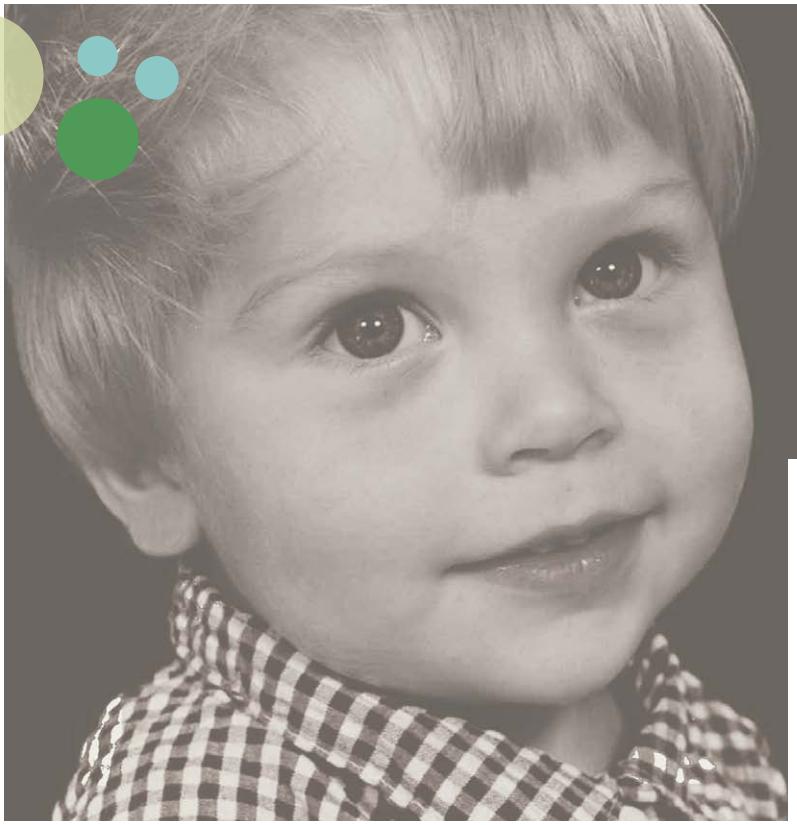
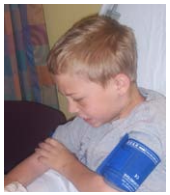
The Foundation for Children with Atypical HUS

www.atypicalhus.org





Nathan

ST LOUIS, MO
DIAGNOSED: 2000
REMISSION/TRANSPLANT WITH SOLIRIS

The Boy Who Started It All. At eleven months old, Nathan was clinging desperately to his mother while medical staff at the hospital ran a multitude of painful tests trying to find out what was causing his lethargic state. No matter how his parents tried to comfort him, the situation got worse. Nathan had no appetite, had extreme pallor, and his kidneys were functioning at about 10%. He was diagnosed with an ultra-rare disease, Atypical Hemolytic Uremic Syndrome (Atypical HUS).

Trying to find help for his son, Bill took to the internet for any information. What he found were just a few medical research papers with very grim statistics and limited treatment options. Fueled by growing frustration, the Biermanns developed the Foundation for Children with Atypical HUS—the goal to provide information to families and doctors, foster community, and help progress research.

Although The Foundation was gaining traction, the next eleven years have remained difficult for Nathan as the disease has asserted itself, over and over, leading him to complete kidney failure, long-term dialysis, and other complications such as seizures, chorea, tube feeds, renal bone disease, and sleep apnea.

Finally, for the first time, Nathan and his family have witnessed new treatment options becoming available—giving them new hope for the future. In September 2011, Nathan received a successful kidney transplant and started Soliris (eculizumab) therapy, with the hope that he will experience a quality of life that he's never known.

ABOVE:
BILL & CHERYL BIERMAN, FOUNDERS, FOUNDATION FOR CHILDREN WITH AHUS

From the Foundation,

Welcome and thank you for your interest in this ultra-rare disease and its effects upon aHUS patients and their families. Atypical Hemolytic Uremic Syndrome impacts lives of children and adults all across the world. For the first time in over 40 years, new treatments are emerging as viable options for individuals with this disease. Our goals as an organization are to support aHUS research, to foster discussion of the most current aHUS medical information, and to increase global awareness of atypical HUS through partnerships with the medical community, universities, aHUS investigators, and corporations interested in medical innovation. We believe that informed patients and aHUS families can join in the discussion of a proactive treatment plan with their medical team—helping to prevent long-term damage and in the end, save lives.

This booklet describes the journey of families affected by Atypical HUS: from a difficult diagnosis, to the search for information and treatment, to hospitalizations, and in some cases the devastating loss of a loved one. Fortunately, with the availability of an effective new treatment, many physicians now consider the disease to be in remission for many patients with Atypical HUS, because the clinical signs and complications of the disease are silent. We invite you to read these stories of courage and learn more about Atypical HUS.

Thank you for your support,

Bill and Cheryl Biermann, Directors
Foundation for Children with Atypical HUS

Linda Burke
Founder of www.atypicalhus.org

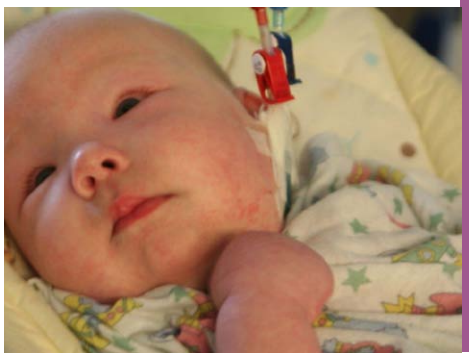
The Foundation for Children with Atypical HUS offers information, support, and resource links for aHUS patients and their families through an interactive website at www.atypicalhus.org, a networking hub linking patients, families, medical personnnel, and aHUS investigators.

Understanding The Difference Between Typical & Atypical

There are two different forms of Hemolytic Uremic Syndrome:

1. **TYPICAL HUS** can be triggered by the E coli bacteria or other bacteria and food borne pathogens. In typical HUS, most cases will not occur again after the initial onset (typically lasting 4-6 weeks). Cases can see long-term kidney damage and issues with high blood pressure.

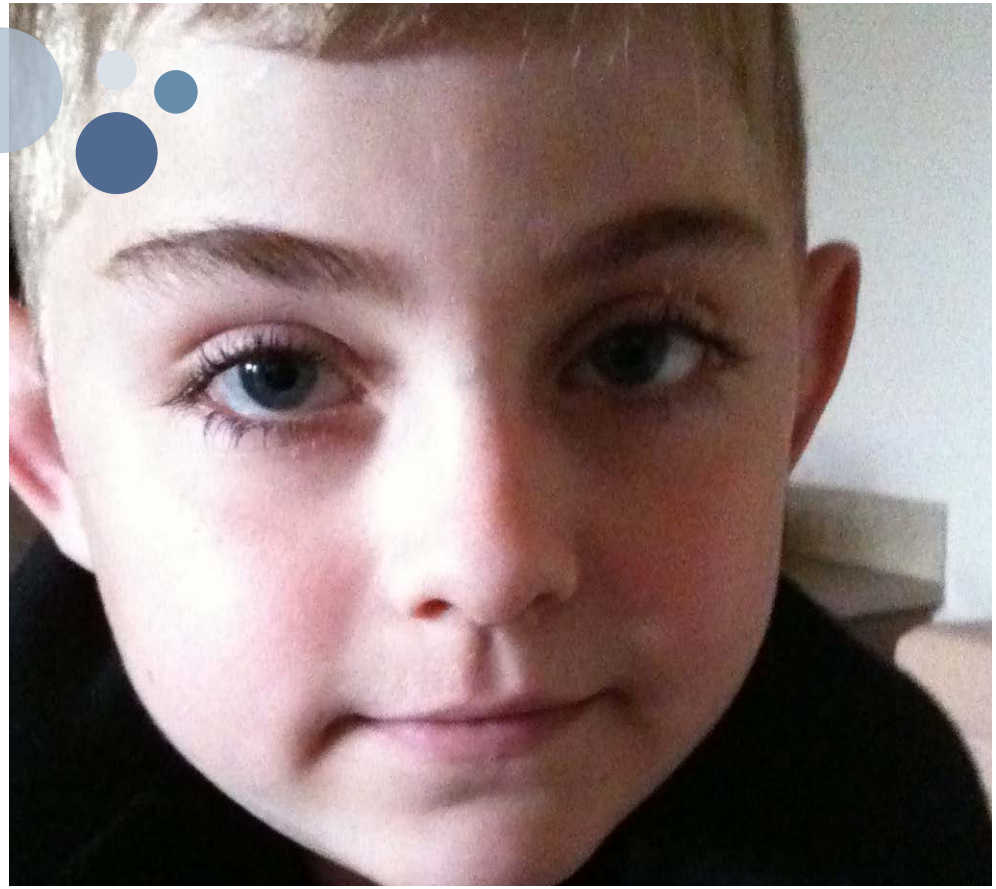
2. **ATYPICAL HUS** is a genetic disease caused by chronic, uncontrolled activation of complement, a part of the body's natural immune system. The disease can be triggered for a variety of reasons, including pneumonia or gastrointestinal illness, or for unknown reasons. Although the symptoms and disease complications are similar, Atypical HUS is known to be very unpredictable with frequent clinical complications—making these cases difficult to manage. Moreover, Atypical HUS is present for life, whereas typical HUS normally does not return after a patient recovers.



Bryan

ATLANTA, GA
DIAGNOSED: 2009
DISEASE STATUS: REMISSION SINCE 2009

A Bright Future for Baby Bryan. At only four months old, Bryan was diagnosed with Atypical HUS. For nearly three months, Children's Healthcare of Atlanta at Scottish Rite would be his new home. The situation was critical—blood transfusions, plasmapheresis, and dialysis treatments kept him alive, yet no treatment seemed to improve his condition. When his kidney function deteriorated even further, Bryan received Soliris off-label, prior to its FDA approval. Being the youngest ever to receive the drug, Bryan surprised everyone by quickly achieving a complete remission. Today, due to early intervention, Bryan is thriving and his kidney function is back to normal. He receives Soliris infusions every two weeks to prevent any possible relapse. Bryan's family, although unsure of what the future holds, is enjoying each happy and healthy moment they share together.



Jose

CASTELLON, SPAIN
DIAGNOSED: 2006
DISEASE STATUS: REMISSION/TRANSPLANT WITH SOLIRIS

In September 2006, it took ten days and three different hospitals for a very sick Jose to be diagnosed with Atypical HUS. Without proper diagnosis and treatment, he reached a stage IV renal failure, and became dependent on dialysis. After being hospitalized and on hemodialysis for three months, Jose was sent home just so his family could take him seventy kilometers, every two days, for treatment.

There was very little information about this disease available to Jose's family, who had an undying dedication to find more answers. In hopes of discovering a treatment option, they consulted with doctors across the world—only to find there were few choices, a double liver-kidney transplant or the not-yet available kidney transplant with Soliris. Not willing to put Jose at risk, they waited a long four years finally to be approved for a kidney transplant with Soliris. Jose's first dose of Soliris was in September 2010 combined with a kidney transplant. Now with his newfound health, he and his family are finally finding peace.

Hemolytic Uremic Syndrome: Understanding the Disease.

Atypical Hemolytic Uremic Syndrome (Atypical HUS) is a very rare and serious disease. Each case of this disease is quite different, making it difficult to diagnose and even harder to treat. Initial symptoms can include extreme fatigue, puffiness, vomiting, paleness, fever, and often diarrhea. These symptoms are chronic in some patients and less frequent in others. Clinical complications of the disease, including kidney damage, can occur even if symptoms are not present. A diagnosis of Atypical HUS can be devastating for a family, often leading to months of inpatient hospital care, long-term dialysis, and a drastic change of lifestyle.

Atypical HUS occurs when the body's immune system inappropriately activates a series of proteins known as complement. This activity produces small blood clots (thrombotic microangiopathy, or TMA) that travel throughout the body.[1,2,3] Often, the blood clots form in the kidneys, where they can lead to severe anemia and kidney failure. When the kidneys fail to work, the body fails to rid itself of toxins, the urine output declines, and the amount of protein in the urine will increase. This process can permanently damage the kidneys. Poorly functioning kidneys also lead to high blood pressure and swelling, which can stress the heart and lungs. Blood clots also may affect the heart and brain, leading to events such as seizure activity, heart attack, or stroke. Atypical HUS and its outcomes are very dangerous and can be deadly if not treated by an experienced physician in a specialized healthcare setting.

A New Hope for Treatment

In 2011, the FDA approved the first and only treatment for Atypical HUS. Known as Soliris (eculizumab), it works by inhibiting uncontrolled complement activation, which helps to reduce TMA and many of the complications associated with Atypical HUS. Soliris is approved for both pediatric and adult patients with Atypical HUS. Clinical trials have shown that Soliris can help reduce the clinical manifestations of the disease and can improve patients' quality of life. The availability of Soliris makes it possible for physicians and patients to consider kidney transplant with less likelihood of the disease recurring in the new kidney.

1. Hosler GA, Cusumano AM, Hutchins GM. Thrombotic thrombocytopenic purpura and hemolytic uremic syndrome are distinct pathologic entities: a review of 56 autopsy cases. Arch Pathol Lab Med. 2003;127:834-839. **2.** Loirat C, Noris M, Fremeaux-Bacchi V. Complement and the atypical hemolytic uremic syndrome in children. Pediatr Nephrol. 2008;23:1957-1972. **3.** Stahl A, Vaziri-Sani F, Heinen S, et al. Factor H dysfunction in patients with atypical hemolytic uremic syndrome contributes to to complement deposition on platelets and their activation. Blood. 2008;111:5307-5315. **4.** Abstract 1587 entitled "A phase II study of eculizumab in patients with atypical hemolytic uremic syndrome receiving chronic plasma exchange/infusion," presented by Dr. Chantal Loirat at the 16th Congress of the European Hematology Association, Sunday, June 12, 2011. **5.** Abstract 1588 entitled "Eculizumab efficacy and safety in patients with atypical hemolytic uremic syndrome resistant to plasma exchange/infusion," presented by Dr. Chantal Loirat at the 16th Congress of the European Hematology Association, Sunday, June 12, 2011.

Atypical HUS: Not Just a Childhood Disease

Atypical HUS is a genetic disease that can be triggered by many causes, including certain bacterial infections, HIV, cancer, organ transplantation, pregnancy, and the use of certain anticancer or immunotherapeutic drugs. Most often, the disease is triggered in childhood but it can also come on during adulthood. Individuals with Atypical HUS frequently relapse even after complete recovery from the presenting episode.

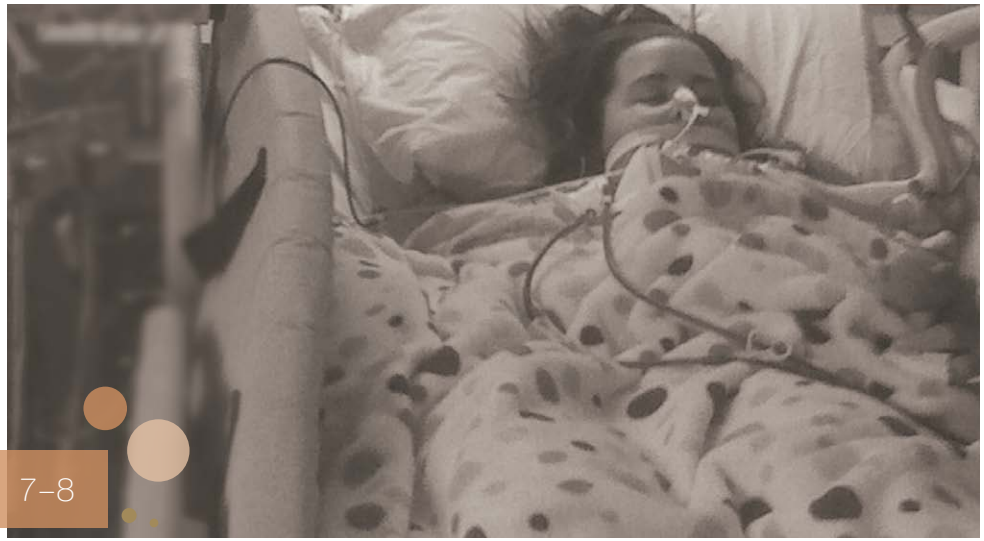
Fighting Her Way Back.

Alyssa was 21 years old when she became ill with what at first appeared to be a stomach illness. A blood test revealed that she had extremely low blood levels and that her kidneys were failing. Atypical HUS struck not only fast, but violently, eliminating her kidney function within ten days of becoming ill. Her condition required immediate dialysis, as well as plasmapherisis to control the hemolysis of blood cells. There were many setbacks including uncontrollable blood pressure, which led to seizures caused by encephalitis. As a last resort to support her organs, Alyssa was intubated and placed in an induced coma.

Alyssa became the 2nd in the world to attempt a kidney transplant combined with Soliris therapy. At 23, she has taken back her life. Alyssa is working again and is thrilled to have the energy level to be able to once again live an active, healthy life.

Alyssa

ROCHESTER, NY
DIAGNOSED: 2009
DISEASE STATUS: REMISSION, TRANSPLANT WITH SOLIRIS

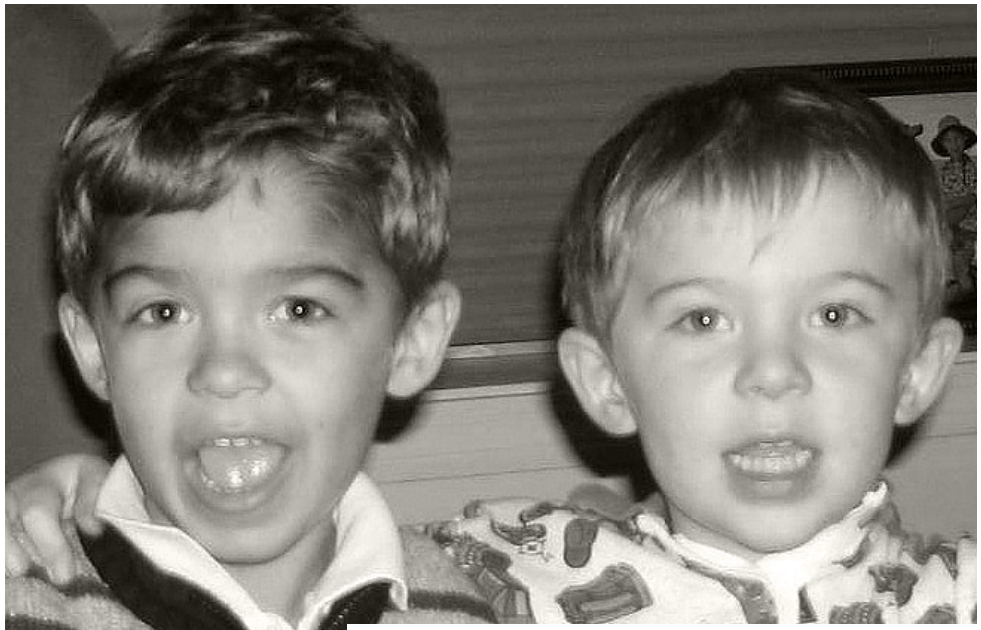


Kamal

ANDHRA PRADESH, INDIA
DIAGNOSED: 1997
DISEASE STATUS: AWAITING 2ND TRANSPLANT

Life's Journey Interrupted. In 1997, at age of 22, Kamal's plans were to attend graduate school in the United States. In preparation for overseas travel, he received three vaccines. Almost immediately, uncontrolled complement activation caused a jolt to Kamal's immune system that cascaded into kidney failure. A renal biopsy confirmed the diagnosis of adult-onset Atypical HUS.

In 1998, Kamal's mother donated a kidney to her son. After just eleven days, the new living donor kidney stopped functioning and a biopsy showed Atypical HUS had recurred—the new kidney was destroyed. Now 34 years old, Kamal spends multiple times each week relying on a dialysis machine to clean the toxins from his body. Despite years of a strict diet and tied for long hours to a dialysis machine, Kamal enjoys his job, travel, and friends. Longing for the opportunity for a second kidney transplant, Kamal awaits the day when laws and regulations allow all nations equal access to Soliris and a better quality of life.



Hunter & Skyler

CAPE ELIZABETH, MAINE
HUNTER: 2003-2008, DIAGNOSED 2003
SKYLER DIAGNOSED: 2008
DISEASE STATUS: REMISSION SINCE 2009

A tale of two brothers. At 10 months old, Hunter was diagnosed with Atypical HUS and over the next four years he would be in the hospital over 600 times. During this period, Hunter was dependent on constant plasmapheresis. At the time, doctors and families did not have a method to share information regarding treatments for this rare disease—including recent success with Soliris. In 2008, Hunter lost his battle with Atypical HUS during an attempted kidney-liver transplant. Shortly after Hunter's death, his little brother Skyler was also diagnosed with the same disease. In April 2009, after 11 days of plasmapheresis and over 40 units of blood, Skyler became 3rd Atypical HUS patient in the world to start Soliris therapy.

Hunter's spirit continues to live on in his family. The interactive website for the Foundation for Children with Atypical HUS was created out of their desire to bridge the knowledge gap between doctors, researchers and families.

As for Skyler, Soliris was a success and for almost two years he has maintained a full remission. Skyler is a happy, active boy who loves music, nature, and outside activities with friends. Celebrating his 7th birthday in 2011, he represents how outreach and communication can save lives.

Who can treat this disease?

Having knowledgeable specialists is critical for successful treatment of Atypical HUS. Typically, a nephrologist (kidney specialist) and oncologist/hematologist are the primary doctors. Other specialists such as cardiologists, immunologists, and intensive care specialists are also involved. Due to the rarity of this disease, many doctors have never had experience treating an Atypical HUS case. Often families have to commute long distances just to receive experienced care.

Genetic Testing

Although Atypical HUS is a genetic disease, many patients do not have a genetic mutation that can be identified.[1] For this reason, genetic testing is not required for diagnosis. However, understanding the genetic components to the disease is important in helping researchers determine future potential treatments. In America, the primary genetic testing facility for Atypical HUS patients is at the University of Iowa. There are only a few other labs across the globe that can perform this testing.

There are a variety of genetic mutations that contribute to aquiring Atypical HUS.

As many as

50%

of patients do not have an identifiable genetic mutation.[1]

1. Noris M, Caprioli J, Bresin E, et al. Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. Clin J Am Soc Nephrol. 2010;5:1844-1859.

Traditional Treatment Options

Although there is no cure for Atypical HUS, the FDA approval of Soliris is bringing new hope to families facing this disease. Prior to the approval of Soliris, the interventions below were commonly used in managing Atypical HUS. The availability of Soliris may change how these interventions are now used:

BLOOD TRANSFUSIONS: Blood transfusions have typically been the first line of management when Atypical HUS patients are admitted to the hospital with anemia. A patient may receive packed red blood cells, whole blood, and/or platelets in order to stabilize their current situation. These products help to return the blood to a more normal level for a brief time but do not treat the disease. During a severe clinical manifestation of TMA, an Atypical HUS patient may depend on hundreds of generous blood donors to stay alive.

PLASMA INFUSIONS: Plasma therapies have been the most traditional way to treat patients with Atypical HUS. With plasma infusion, donated plasma is transfused into an Atypical HUS patient.

PLASMAPHERESIS: In difficult cases, plasmapheresis, a process where the body's plasma is removed and replaced with donor plasma, may be used instead of plasma infusion.

DIALYSIS: Atypical HUS can cause a patient's kidneys to permanently or temporarily stop functioning. If the patient's kidneys cannot perform properly, patients must receive dialysis. Dialysis can be used as an interim replacement for kidneys. Though it is necessary to sustain life, dialysis can be risky for young patients. Due to the ongoing nature of the disease process and subsequent damage to the kidneys, nearly all Atypical HUS patients are on extensive blood pressure medications as well as other medications that help regulate the body's ability to manufacture red blood cells and ability to regulate electrolytes.

KIDNEY TRANSPLANTS: Many Atypical HUS patients have permanent kidney failure. Kidney transplants have not historically been an option for these patients due to a high rate of disease recurrence. Today, the availability of Soliris makes it possible for physicians and patients to consider kidney transplant with less likelihood of the disease recurring in the new kidney.

KIDNEY/LIVER TRANSPLANTS: For some mutations, such as Factor H mutation, a kidney/liver transplant has been used with success. However, there are great risks associated with a dual transplant and mixed views from the medical community about the viability of this option.

Coen

SPOKANE, WA
DIAGNOSED: 2003
DISEASE STATUS: REMISSION SINCE 2009

A Birthday to Remember. On Coen's first birthday, he nearly lost his battle with Atypical HUS. He had been hospitalized for nearly a month when complications of the disease caused his lungs to fill with fluid, taking away his ability to breathe. Though the medical staff at Sacred Heart Children's Hospital saved his life that morning, he didn't go home for another three months. In the next five years, Coen received over 400 plasmapheresis, countless immunosuppressant therapies, and months of dialysis—never achieving remission. In early 2009, when the disease flared worse than ever and the conventional therapies didn't seem to be working, Coen became the first in a handful to try Soliris, off-label at the time, for the treatment of Atypical HUS. Since then, there has been no further sign of destruction of Coen's blood cells, and he has regained much of his kidney function. For the first time ever, his life is seemingly normal. In between recess, Legos, and playing with his new puppy, Coen squeezes in time for his monthly infusions—making certain no Atypical HUS relapses are in his future.

Hyde

CUMMING, GA
DIAGNOSED: 2008
DISEASE STATUS: REMISSION, TRANSPLANT WITH SOLIRIS IN 2011

Setting the Standard. Little did Hyde's family know that a trip to the emergency room in January 2008 would launch a nightmare of hospitalizations, invasive treatments, and emergency ambulance trips—due to a diagnosis of Atypical HUS. Hyde's treatments included blood transfusions, platelet transfusions, continuous veno-venous hemofiltration therapy, plasmapheresis, hemodialysis, and even a ventilator for a week due to fluid overload.

After a six month rollercoaster, Hyde's genetic testing confirmed he has a mutation of Factor H, meaning a kidney transplant would not be an option due to nearly certain recurrence. For the next 3 years, Hyde was on peritoneal dialysis with no options.

After years of research and strategy, and because of the willingness of his uncle to donate, Hyde became the 3rd person in the US (and the youngest by far) to undergo a kidney transplant along with Soliris therapy in February 2011.

Today, Hyde is a happy energetic boy who is busy planning his 5th birthday pool party—an option for the very first time.

Prior to 2009, approximately, 90% of kidney transplants for HUS patients, resulted in relapse of the disease.

A Brighter Future Awaits. As a newly graduated and licensed Veterinary Technician, this Atypical HUS veteran has triumphed over the challenges that have faced her. Now 23 years old, Jessica lost all kidney function as a baby and has spent a life defined by the rigors of the dialysis schedule. Diagnosed with Atypical HUS at 11 months of age, Jessica spent two months in ICU, her fighting spirit honed by battling astronomically high blood pressures. Whether expressing herself through reflective forms of artwork or the excitement and activity of a dance recital, Jessica exemplifies the passion for making the most out of each moment.

Jessica had fond memories of her girlhood Make-A-Wish trip to Disney World, and as a young adult she recently returned to Florida with college friends to swim with the dolphins—transitioning from children's hospital wards to adult dialysis units along the way. Though her path in life has been filled with unexpected twists and barriers, Jessica hopes that a successful transplant will ensure that she'll journey along a smoother road toward a happy beginning.

Jessica

BUFFALO, NY
DIAGNOSED: 1989
DISEASE STATUS: 22 YEARS ON DIALYSIS, AWAITING TRANSPLANT

About The Foundation for Children with Atypical HUS

The Foundation for Children with Atypical HUS is a 501c3 nonprofit organization dedicated to helping patients and families affected by this disease. Our three primary goals of the organization are: to provide information to patients and families about this ultra-rare disease, to provide support by establishing a global network so interested individuals can communicate with one another to exchange opinions and experiences, and to provide funds for medical research to offer improved prognosis for aHUS patients. The Foundation for Children with Atypical HUS encourages patients and investigators to share information and explore options/resources as we work together to gain insight into this rare and complex disease. By increasing contact opportunities with researchers and medical personnel interested in helping the aHUS community, our stories foster a better understanding of atypical hemolytic uremic syndrome. Sharing information, inspiration and support for one another, we seek to gather together people and knowledge as we strive to improve the lives of patients and families dealing with aHUS.

Join the community at: www.atypicalhus.org.
More info at www.atypicalhus50megs.com.

Bill Biermann, Director
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In partnership with University of Iowa:
www.uihealthcare.com/depts/uitransplantcenter/index.html

DONATE LIFE

Photos: HUS patients and families, used by their permission. Symbology: The colored bubbles represent aHUS patients, recognizing both those living with strength and courage as well as honoring the cherished lives lost to aHUS. Dragonfly is a transformational symbol and a reminder of love and the power of life. A butterfly might appear to be fragile but has great inner strength, and so is often used as a symbol for organ donation. We include the butterfly to honor all the wonderful organ donors who cherished life so much that they unselfishly wished to 'Donate Life' and renew/transform/enrich the lives of others.

Brochure created by Jodi Kayler, an aHUS parent along with Linda Burke, founder of www.atypicalhus.org. Authorized by Bill and Cheryl Biermann, co-founders of The Foundation for Children with Atypical HUS (2011)

For information on Genetic Screening for aHUS:

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