The purpose of The Henry Loring Masters Foundation, Inc. is to honor the memory of our son, Henry, by building awareness of best medical practices for the illness that led to his death at age 25 in November 2009. The ultimate goal is better outcomes for others afflicted with such autoimmune disorders.

A student, teacher, and mentor, Henry had already made a significant impact in various communities. His was a life of great promise, and we feel the loss of him and his potential profoundly. Through this foundation, we honor his capacity to effect change—in this case, to eliminate the fact that limited information exists on autoimmune hemolytic anemia (AIHA) in teenagers and young adults, and to improve on how practitioners should treat afflicted patients.

Henry died during his second fight with idiopathic AIHA, and no underlying cause for his hemolytic anemia was ever identified. Henry initially presented in Boston, just before his high school graduation, at which time arrived in the Children's Hospital Emergency Department with a severe case of jaundice. He was diagnosed with AIHA quickly, and his initial treatment course included standard-of-care measures such as steroids, and intravenous gamma globulin. While there were some temporary responses, Henry continued to break down his red blood cells, requiring almost twenty units of blood over his first few weeks of care. Finally, when removing his engorged spleen failed to stem the tide of massive hemolysis, Henry was treated with an emerging therapy called rituximab. Thankfully, Henry showed a positive and lasting response to this infusion, which is given four times over one month. After making a full recovery, Henry went on with his busy lifestyle, and the memories of his battle with AIHA began to fade into the past.

Fast forward seven years to November 2009. Henry had finished college, and after considering veterinary medicine and law school and building an impressive nonprofit resumé, he was approaching the halfway point in a graduate program in public health policy at Dartmouth College. He had been home for the weekend with a Dartmouth classmate, and he felt the onset of a cold or flu as he headed back to school. When he awoke the next morning sick and with jaundice, he drove himself to nearby Dartmouth-Hitchcock Medical Center. Although a relapse of his hemolysis was unexpected, Henry knew his AIHA had returned.

Despite aggressive intensive care and multispecialty support, Henry died five days later, in the early hours of Saturday November 21, 2009, at the age of 25. After his death, laboratory analysis confirmed the suspicion that he had contracted Type A Influenza/H1N1, or the so-called "swine flu." It is believed that the H1N1 attack on his immune system was vigorous enough to trigger his autoimmune response.

A possible complicating factor in his second illness was that he no longer had a spleen. It had been removed as part of his treatment in 2002. Another

contributing factor was the fact that it was extremely difficult to match his blood for transfusion, since his prior history in 2002 exposed him to many different blood surface antigens, complicating the search for compatible blood.

Autoimmune hemolytic anemia, although well known in the medical community across a wide range of ages and circumstances, is not well understood, diagnosed, or treated when it presents in young adults. It occurs seldom enough in this age group that practitioners might see it only once or twice in their career. The chances are slimmer at smaller or rural medical facilities.

AIHA can be very aggressive and therefore needs to be diagnosed quickly so that appropriate therapy can be instituted and modified, if necessary. Complicating the diagnosis is the fact that anyone can present at any time with anemia from a very wide range of causes. In addition, jaundice has many etiologies, and in the patient presenting with anemia, many other contributing factors need to be considered. But because of its potentially aggressive nature, any young adult presenting with jaundice or other signs of hemolysis, such as a dropping red blood cell count, an enlarged spleen, or dark urine, needs to be considered an AIHA patient until proven otherwise. As with other rapidly progressive conditions, such as myocardial infarction (heart attack) or cerebral ischemia (stroke), AIHA should be treated as a medical emergency, and the proper diagnostics and support systems should be mobilized with urgency.

In simple terms, AIHA results when the body's immune system begins to recognize "self" as it would a foreign invader, such as a virus or bacteria. When red blood cells are targeted by the immune system, the body's natural response is to destroy those cells, as it would any pathogen. Hemoglobin spilling out of these destroyed red blood cells is metabolized by the liver, resulting in jaundice. In a previously healthy person with a strong immune system, the red cell destruction can occur at a catastrophic rate, overwhelming the body's ability to produce more red blood cells. In fact, the same destructive process can target the immature red blood cells produced by the bone marrow, compounding the problem. There have even been reports of a complete shutdown of red cell production, leaving the body in a hyperactive state of destruction without any means of making more red cells to deliver oxygen to vital tissues and organs.

The Coombs blood test is the definitive means of establishing the diagnosis of AIHA. While a standard laboratory test, it requires special equipment, and interpretation of results can require a degree of expertise. The test reveals whether the immune system is coating the red blood cells with the proteins that flag them for destruction.

Traditional treatment protocols are aimed at modulating and "cooling off" the immune system. As such, the mainstay of therapy remains corticosteroids, which are very effective in dampening the immune response. As with any immune-modulating therapy, results are not instantaneous, and there is a delay from the

time of therapy initiation until a response is observed. Since the spleen is one of the body's primary agents for removing the targeted red blood cells, the next step in therapy often is to remove this organ. While this is curative for some, it renders the patient (especially children) more susceptible to infection with certain kinds of bacteria, and therefore lifelong immunization against these organisms is recommended.

More sophisticated and targeted means of immune modulation have emerged over the past decade, and one such agent was used for Henry in 2002 when other methods failed to slow the tide of red cell destruction. Rituximab is an antibody that targets a receptor on the surface of B-type white blood cells, exactly the culprit that helps target the red blood cells for destruction. Of course, this B cell destruction is indiscriminate, leaving the patient at an increased susceptibility to infection for months. Once one or more of these maneuvers has stemmed the tide of hemolysis, the body can begin to compensate and slowly regenerate the pool of circulating red blood cells.

The use of these more sophisticated immune-modulating agents has yet to be studied in any systematic way as front-line therapy for AIHA. Given the relative ease and mostly benign side-effect profile for corticosteroids, and the fact that most patients respond to conservative measures, it would be difficult to argue for agents such as rituximab as first-line therapy. Nevertheless, for some, the presentation of AIHA can be aggressive and fatal, possibly requiring a multifaceted therapy approach, including the front-line use of immunosuppressants such as rituximab. Because of its extremely low incidence in young adults, a large multi-arm trial studying these options would be difficult or impossible.

However, it is obvious that the timeline is key, and that rapid diagnosis and treatment can make a huge difference in outcomes. This is where the foundation can and intends to make a difference.

This foundation has set its objectives in four key areas for its initial work.

One.
We will bring together a select roundtable of researchers, physicians, practitioners, and other interested professionals each year at an annual global conference of hematologists to share clinical data and best-practice outcomes by case study and clinical presentation. It is our plan to work with the American Society of Hematologists (ASH) in establishing an annual "Roundtable on AIHA in Young Persons" session during the society's annual meeting, starting in 2011.

Two.
We will launch a campaign to alert staff in emergency rooms, regional trauma centers, college and school infirmaries, and other places where first responders may be unaware of the need for proper diagnosis and early intervention in young

adults. Among the elements of this campaign will be a well-designed poster or bulletin board notice that gives basic information and directs the reader to additional resources.

Three.
We will build a web presence that aggregates information for clinicians and laypersons. Over time, we hope to build a library of data and papers, presentations and case studies, or linkages to libraries of materials that offer best practice and objective information. We will encourage participation in such a virtual library by both the medical community and patients and families who need guidance.

Four.
We hope to form a community for families and patients who want to develop a better understanding of what they are facing. We faced our fears in a virtual information void, and we would therefore like to connect with the community of those who have experienced this condition. Hopefully, new people will join us to help us grow and change, making us more effective in striving to build the awareness that leads to better outcomes.

We have appointed a board of directors whose members encompass clinical understanding of AIHA, not-for-profit board-level and/or governance experience, and direct or indirect relationships with Henry. Two members are Henry's friends, one in medical school and one planning to attend medical school. They will keep us in touch with new media/communications tools and ideas, and keep us true to Henry's demonstrated capacity of the power of entrusting young adults with responsible leadership roles. We are confident we have found the proper balance of knowledge, wisdom, commitment, and youth.

The foundation hopes to attract and involve new families to participate in and perhaps even manage this foundation someday. We seek to reach a broad number of people who have the potential to change outcomes for young adults with AIHA and to help their families through this difficult disease. We know we can guide clinical staff toward best practices and better outcomes for AIHA patients by systematically sensitizing providers to the danger of moving slowly and to the risks of relying only on their institution or discipline's default treatment.

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