

## High Time for HiCy?

Contributed by Elaine Freeman - Hopkins Medicine Magazine  
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Convinced they hold the cure for a host of autoimmune diseases, Hopkins researchers have refused to give up in the battle for acceptance. Now success is in sight.

Becky Lovelace was living on transfusions and losing blood almost as fast as she received it. It was 1977, and life expectancy for patients with severe aplastic anemia was a year, unless they had a matched bone marrow donor. Becky, 24, had no donor and had failed all standard treatments.

That was the grim picture when her desperate parents brought her to Lyle Sensenbrenner at Johns Hopkins Hospital. He had just one possibility to offer, and it was a long shot: high doses of cyclophosphamide (HiCy) could destroy Lovelace's bone marrow, the factory for her blood cells, and whatever was causing her body to attack them. Then, if she were lucky, a healthy immune system might reboot.

The theory was untested, but it seemed to explain an unexpected observation in another patient with severe aplastic anemia (SAA)—a 19-year-old who had received HiCy to prepare him for a bone marrow transplant from his sister the year before. The transplant hadn't taken. As his blood counts recovered post-transplant, they were not his sister's cells, they were 100 percent male, his own cells—but they had recovered. Perhaps, Sensenbrenner mused, cyclophosphamide alone was responsible for the cure.

He had to be candid with Lovelace: "This treatment may kill you faster than your disease." Despite the great risks involved—Lovelace would be gravely vulnerable to infections for weeks—she and her parents agreed to the experimental treatment. For four consecutive days she received HiCy infusions, suffering the acute toxicity familiar to patients on chemotherapy. Then for two weeks she had very few red blood cells, white cells, or platelets. "I was chewing my fingernails down to the cuticles," Sensenbrenner admits. "Finally, after two weeks her blood counts began to go up, at first gradually and then faster. We breathed a tremendous sigh of relief."

Over the next decade, Sensenbrenner used HiCy to treat 10 patients with this often fatal disease. But when he left Hopkins in 1987 to accept a job in his native Michigan, the series stopped—and so did any follow-up to determine long-term outcome.

That's how things stood in 1994 when Robert Brodsky finished a fellowship in hematology at the National Institutes of Health and was hired by Johns Hopkins for an oncology fellowship. Casting about for a clinical project for his newest protégé, who had a long-standing interest in aplastic anemia, Richard Jones, director of the Hopkins bone marrow transplant program, suggested that Brodsky track down the original 10 HiCy patients.

What Brodsky found, he recalls, was "shocking." Not just that six were alive and well (a seventh had died not from SAA but from transfusion-transmitted AIDS). "But their blood counts were normal. We weren't used to seeing such counts even with patients who responded to standard therapy." And unlike patients on standard therapy (ATG or cyclosporine), the HiCy group hadn't been on any immunosuppressive medications for a decade. Seven of the 10 had been cured of aplastic anemia by HiCy. With the evidence so clear, it was more than time, Brodsky and Jones realized, to start investigating HiCy seriously as a cure for SAA—and potentially for the 80 other autoimmune diseases (from multiple sclerosis to myasthenia gravis) that plague more than 8 million Americans.

They immediately launched a new study, and five years later, in 2001, published results showing they had cured 12 of 19 additional SAA patients treated with HiCy. After the article appeared in *Annals of Internal Medicine*, rejoicing seemed in order. Indeed, this magazine celebrated the accomplishment with a cover story.

Surprisingly, the article drew strong responses, both positive and negative, from distinguished School of Medicine alumni who received the magazine. One called Hopkins to learn more about the treatment Brodsky and Jones were pursuing, then told anyone who would listen, "I can't name another Hopkins contribution to clinical medicine that comes close to matching this technology," said this successful entrepreneur. "If these guys don't pick up a Nobel Prize someday, I will be shocked."

But among some members of the medical community outside Hopkins, there was strong opposition to using HiCy as a treatment for autoimmune diseases. Researchers at the NIH had conducted a randomized trial, reported in *Lancet* the prior year, which had been prematurely terminated. The reason? The treatment had proved too toxic, they said, and entailed "much higher requirements for supportive care."

Brodsky and Jones launched an effort to defend the Hopkins protocol. In letters to the editor of *Lancet* and *Annals of Internal Medicine*, they pointed out that the NIH study differed from the Hopkins approach. NIH researchers started cyclophosphamide concomitantly with another drug [cyclosporine] that "may increase toxicity" and block

“a potential mechanism of action for cyclophosphamide.” But the damage to more widespread acceptance of HiCy treatment was done.

Gloom. Brodsky and Jones knew their treatment would never emerge from under the radar screen without a convincing, multi-center, randomized trial. Such trials are so expensive, only two sources have the deep pockets to fund most of them: the government (usually the NIH) or a pharmaceutical company. With no apparent intellectual property to license—cyclophosphamide was a generic compound, off-patent for 30 or 40 years—cross out the pharma funding route. That left the NIH as a logical source for funding.

Neither Jones nor Brodsky was prepared for the response to their grant application from the NIH study section, though perhaps they should have been. Not only was the Hopkins proposal roundly rejected, one reviewer asserted that to conduct the study would be “unethical.”\*\*\*\*At other institutions, with both the NIH and pharma funding doors closed, that might be the end of the story. Fortunately for Jones and Brodsky, at Johns Hopkins they were surrounded by a community of clinician-scientists who shared their passionate belief that autoimmune diseases can be cured—not just treated but cured, or at least put into remission for extended periods—using the disputed HiCy protocol. (See “What Does ‘Cure’ Really Mean?” sidebar.) Neurologists, dermatologists, rheumatologists, each had published pilot studies with Brodsky documenting the protocol’s success with conditions ranging from lupus to multiple sclerosis, from scleroderma to myasthenia gravis.

There was general agreement among the Hopkins doctors about an important nuance (in addition to the altered drug protocol) separating their trials from the one at the NIH that had fared so badly: a system in place to provide the “much higher requirements for supportive care” during what could be a very rough and lengthy recovery period. HiCy treatment is not for the faint of heart. Because it wipes out the bone marrow and leaves patients with no functioning immune system, it leaves them vulnerable to any passing germ, virus, or fungus, until their stem cells can reconstitute bone marrow and blood products.

“The secret weapon here,” says Hopkins neurologist Daniel Drachman, “is IPOP,” the inpatient/outpatient care continuum program at Hopkins’s Sidney Kimmel Comprehensive Cancer Center. Whatever their autoimmune disease diagnosis, and whoever their admitting physician, patients receiving HiCy treatment were overseen by the bone marrow transplantation (BMT) service and IPOP nurses accustomed to caring for people undergoing extreme courses of chemotherapy. During treatment, these patients live in nearby residences, returning daily to the same care team for testing, for prophylactic antibiotics, and for growth factors to stimulate bone marrow recovery.

“These patients must be under surveillance seven days a week until their blood counts come back up,” says Drachman, who has been working to eliminate myasthenia gravis (MG) for the last 25 years using HiCy. “If they crash on a weekend, there must be someone who knows what to do.” With the slightest fever, they’re readmitted to the hospital and aggressively treated. Risk management—informed by three decades of institutional experience administering the HiCy treatment—is a vital part of the Hopkins protocol.

Determined not to give up, Hopkins clinician-scientists decided to try a different strategy to gain funding for a multi-center trial: Avoid severe aplastic anemia, the focus of the disputed studies, and focus instead on a different autoimmune disease. Multiple sclerosis (MS), striking approximately 400,000 people in the U.S. each year, offered the best chance for recruiting enough patients to complete a definitive study in a reasonable length of time. And Hopkins researcher Douglas Kerr had preliminary results showing HiCy could do better than just slow progression of the debilitating disease—it could potentially cure it. (See “Like Stomach Flu with a Goal,” below.)

Another good reason to shift to multiple sclerosis: the duration of low blood counts following HiCy treatment for autoimmune conditions other than SAA is much shorter, leaving patients far less vulnerable. That’s because the immune system’s targets in SAA are the stem cells required to regenerate bone marrow.

Hopkins researchers and others had discovered in the 1980s that while HiCy destroys most of the body’s blood cells—and with them the out-of-whack immune system—stem cells are protected by an enzyme, aldehyde dehydrogenase, that inactivates cyclophosphamide.

“Patients with aplastic anemia come in with neutropenia [no red cells, no white cells, no platelets],” explains Brodsky. “Their bone marrow is practically wiped out of stem cells, while in other autoimmune diseases, patients have hundreds of times more stem cells to start with.” Consequently, says Brodsky, “the average time blood counts are down in patients with multiple sclerosis is only eight days, versus 50 with aplastic anemia.”

Together neurologists Kerr and Drachman wrote the clinical trial grant application, with Kerr to serve as principal investigator. He submitted the application to the NIH once, and was rejected. A second time: rejected. Application to the National Multiple Sclerosis Society: rejected. Each time the concern was about patient safety. “One reviewer said it was ‘too risky an approach for a disease such as MS,’” recalls Kerr, shaking his head. “But MS is a devastating disease. As one of my patients said, ‘Mortality is not defined by stopping of the heart, but by when you can’t do things that mean a lot to you in life.’”

Nevertheless, "after three rejections," says Kerr, "we were pretty much done. We didn't know how we'd do the multi-center trial on our own." It was 2005, and his grant applications, as well as Brodsky and Jones's, had been turned down. Only a gift from a local philanthropist was allowing a small trial of HiCy against MS to proceed.\*\*\*\*At this point, an unexpected player re-entered the scene: Frank E. O'Donnell Jr., the entrepreneurial alum, who had pinned such high hopes on the protocol.

"He's the total package," says Wilmer Institute Director Peter McDonnell. "He's brilliant and has succeeded in multiple venues: ivory tower, business, practice. He had a stellar career here, and his professors hoped he'd continue in an academic career. But he's also a tough, focused businessman, and a lot of academics have a problem with that."

O'Donnell came to the Johns Hopkins accelerated program in 1971 after two years at St. Louis University, received his Hopkins B.A. in 1972 and M.D. in 1975, did his internship in Florida, then returned to Hopkins for training in ophthalmology and plastic surgery. At 29, he completed the Wilmer chief residency and left to become chairman of ophthalmology at St. Louis University.

At some point, O'Donnell decided he wasn't "bright enough to be a discoverer," but recognized that he was good as an "enabler." Starting off as a "passive" medical venture capitalist, he helped bring to market "lasik," laser eye surgery to reduce dependency on glasses or contact lenses. Then 10 years ago, at age 48, O'Donnell started devoting all his efforts to technology transfer and formed his own company, Hopkins Capital Group (HCG), a privately held limited partnership that serves as an umbrella for niche pharmaceutical firms. "It's not a career path I would have predicted," he says, "but I love what I'm doing."

The tag line of O'Donnell's new company: "Key Funding for Disruptive Technologies." Just as lasik "disrupted" the way vision problems are corrected, creating an opportunity for a specialized laser manufacturer, "if a little company can get FDA approval," O'Donnell maintains, "it can drive the field, as there's no competition."

One of the companies in HCG's portfolio, Accentia Biopharmaceuticals, acquires what it perceives as disruptive drug products in late-stage clinical development. Based on ingredients already approved by the FDA for other indications, these products usually are eligible for an accelerated regulatory approval pathway.

"From the time I first read about Rob and Rick's work," says O'Donnell, "I was convinced that this was a very, very important advance in clinical medicine." For someone interested in profitable disruptive technologies, the lure of HiCy as a treatment for millions of people with autoimmune diseases was tantalizing: "Let's not treat autoimmunity," proclaims O'Donnell. "Let's eliminate it and restore function!" Ever the entrepreneur, he likes to describe HiCy as "16 hours to a cure: four hours a day for four days in a row."

To some, the business challenges of bringing this product to market might have seemed overwhelming: apparently no intellectual property to license and a technology requiring considerable clinical trial expenses for a generic drug.

"I was slow about solving the obstacles," admits O'Donnell, "but I was also not going to give up. I kept in touch with Rob and Rick periodically as I noodled on trying to solve these barriers. It took me a few years, but I came up with a commercialization strategy based on the need to implement a system of care...to ensure patient safety." The costs of the medicine and of a risk management program would be bundled together.

Thalidomide had served as a precedent. Abandoned for decades after research linked its use in pregnant women to birth defects, thalidomide had moved out of the shadows and gained approval as a treatment for leprosy and for multiple myeloma. Coupled with a risk management package, it was now being marketed as "Thalomid."

As O'Donnell saw it, "The outstanding safety profile achieved at Hopkins was the result of a systematic approach" to minimize morbidity, i.e., the nuances. He believed he could make this "system of care" an integral part of a patent and of a new drug application to the FDA.

When he returned to Brodsky with this plan in 2005, he was met with skepticism. "It didn't make a whole lot of sense to me," says Brodsky. "I pulled Rick in, and it didn't make sense to him, either, so we pulled the tech transfer people in, and they said O'Donnell was legit." Furthermore, he was willing to "de-risk" the next steps for Hopkins by agreeing to pay up front for all patent drafting and prosecution.

O'Donnell's company ultimately selected a "process patent" similar to the route used to patent new applications for thalidomide. They branded HiCy as Revimmune and determined to move forward using multiple sclerosis as the focus for a proposed large-scale clinical trial.

Throughout the past year, a string of press releases from Accentia traces Revimmune's path to market, from acquisition of "exclusive worldwide rights for Revimmune" to a pre-Investigational New Drug (pre-IND) meeting with the FDA. The results of that meeting, says Kerr, were encouraging: The FDA indicated its support for Accentia to submit an IND for a Phase 3 clinical trial of Revimmune among patients suffering from an aggressive form of multiple sclerosis known as refractory, relapsing-remitting MS (RRMS).

What makes this MS trial different from any other filed with the FDA, says O'Donnell, is that it will use "restoration of function" as its endpoint. That's based on results of a pilot study by Kerr that used HiCy to treat nine patients with RRMS—patients for whom all other treatments had failed.

"I thought at best we'd see no increased disability," says Kerr. "Instead, we demonstrated a 41 percent average reduction in disability—a reduction that persisted. Pretty heady stuff considering that the most potent therapy for MS on the market shows a 17 percent increase in disability over two years," says Kerr.

Brodsky and Jones now have their names attached to what might become a blockbuster drug patent, but remain bemused skeptics about its commercial viability. "I still don't know how they'll make money from something that's been off-patent for 30 or 40 years," says Jones. "But if filing for a patent was the only way to get a drug company interested enough to fund a big trial that might get the treatment out there, I was willing to go along."

Brodsky concurs: "If it leads to a trial in MS that truly tests the treatment in a multi-institutional, randomized way, it will be worth it and will teach us things like whether HiCy should be used earlier or later in MS."

Under conflict of interest regulations, neither Brodsky nor Jones will be allowed to "consent" patients in the MS trial, but can treat them if supportive care is needed, and, of course, now must include a disclosure statement with their publications. \*\*\*\*\*Last year, Hopkins sponsored a reunion to thank patients who had the HiCy treatment over the past 30-plus years. Among those present was petite Becky Lovelace, today 54 years old and working in a car dealership after a career that's run the gamut from pumping gas to teaching, from repairing computers to wearing a hardhat in a steel mill. Her presence was stark evidence that, for some, HiCy truly is a cure, not just a treatment.

"I didn't know I was the first until the reunion," Lovelace confided recently. "Dr. Sensenbrenner took me aside and said, 'If you hadn't lived, I wouldn't have continued my research and none of these people would be here today.' It gave me chills to think I was part of something so big, that my life was really worthwhile."

For HiCy champions, the prospect of achieving broader acceptance for a treatment that's helped close to 100 Hopkins patients with auto-immune diseases since 1977 seems closer than ever. But everything is relative. Although the pre-IND meeting at the FDA went well, Accentia probably won't submit the IND application until early in 2008. Then comes the 30-day wait for the FDA's response. Even if the FDA were to approve a clinical trial tomorrow, says Kerr, it would still take about a year to launch.

"Both Accentia and we at Hopkins have a lot of work to do. For example, we have to establish what centers have the competence to participate. We have to get personnel on the ground familiar with the protocol at each center and work with them on IRB submissions." To recruit approximately 270 patients with RRMS for the trial, Kerr estimates, "We need to get 12 to 15 groups throughout the country attached to a center such as the Hopkins BMT service that can provide intensive supportive care. Otherwise, a patient could die from a fulminating infection." But he's optimistic. At an October meeting of the American Neurological Association, where he shared his recent results, neurologists from 20 centers expressed interest in joining the trial. So perhaps the tide finally is turning.

While Kerr prepares for the big clinical trial, Brodsky, Jones, and their BMT colleagues Ephraim Fuchs and Leo Luznik continue to work on new uses for HiCy, particularly ways to enable transplants from partially matched (haploidentical) donors without triggering graft versus host disease (GVHD). Two days of HiCy therapy three days after bone marrow transplant, for instance, cured sickle cell anemia in a young woman who had spent much of her life going in and out of hospitals. "Now any sickle cell patient who has a parent, child, or living sibling," Brodsky beams, "is a transplant candidate! A half match is good enough."

What's sexy in science these days is treatment with stem cells. But Brodsky would tell you HiCy is treating patients with stem cells. They're there; they're the patients' own stem cells. They just need to be protected from attack by an out of whack immune system and given the chance to regenerate. That is exactly what HiCy accomplishes.

Ironically, the struggle to gain acceptance for HiCy as a cure for autoimmune diseases parallels a much earlier struggle to convince the scientific community such conditions even existed. The "bible" of the field, The

Autoimmune Diseases (now in its fourth edition and co-edited by Hopkins's Noel Rose), opens with a chapter by immunologist/medical historian Arthur Silverstein titled "Autoimmunity: A History of the Early Struggle for Recognition";

"It is one of the curious situations in science," begins the chapter, "that certain well-demonstrated facts are refused entry into the body of accepted knowledge, and may become so effaced from the collective memory that they must be rediscovered many years later in order to gain acceptance. Such was the case in immunology... In the end, it may be that... acceptance of a fact in science depends less upon its truth than upon its acknowledgment by the leaders in the discipline"; However, the truth in science ultimately emerges, although sometimes it takes a very long time. Under a licensing agreement between Accentia Pharmaceuticals and the Johns Hopkins University, Drs. Brodsky and Jones are entitled to a share of royalty received by the university on sales of intellectual property (Revimmune). The study described in this article could impact the value of Revimmune. The terms of this arrangement are being managed by the Johns Hopkins University in accordance with its conflict-of-interest policies.

#### HICY AT HOPKINS: A TIMELINE

"It takes 50 years to get a bad idea out of medicine and 100 to get a good idea in." —Hughlings Jackson

"We're almost half way there." —Richard Jones

1969: George Santos proves high-dose cyclophosphamide (HiCy) is toxic to diseased marrow and suppresses the immune system prior to bone marrow transplant (BMT).  
 1976: Severe aplastic anemia (SAA) patient treated with HiCy prior to bone marrow transplant from sister recovers, but, unexpectedly, with his own cells.  
 1977: First SAA patient purposely treated with HiCy without bone marrow transplant.  
 1977–87: Ten patients treated with HiCy for SAA.  
 1980's: Scientists show mechanism by which stem cells—but not lymphocytes—survive HiCy, allowing "rebooting" of naïve immune system.  
 1982: Studies of HiCy for myasthenia gravis (MG) start in animals.  
 1987: Lyle Sensenbrenner leaves Hopkins; SAA series stops.  
 1994: Robert Brodsky and colleagues start follow-up of 10 SAA patients.  
 1996: Pilot study results published, showing 7 of 10 patients "cured."  
 1998: HiCy success against lupus pilot study published.  
 1999: HiCy success against pemphigus published.  
 2001: Results from 19 SAA patients published, showing durable, treatment-free remission in 65 percent.  
 2001–07: Publications document HiCy success against post-transplant graft versus host disease, autoimmune hemolytic anemia, refractory myasthenia gravis (MG), multiple sclerosis (MS), lupus, scleroderma, other autoimmune diseases.  
 2002–05: NIH rejects clinical trial grant applications for HiCy vs. SAA and MS.  
 2006: HiCy patent application filed.  
 2007: Accentia licenses HiCy, names it Revimmune, and plans to file pre-investigational new drug application with FDA for Phase 3 clinical trial for MS.

#### WHAT DOES CURE REALLY MEAN?

The word "cure" is a tricky thing. "HiCy is a cure, like bone marrow transplant is a cure," says Hopkins hematologist Robert Brodsky. "There are aplastic anemia patients who are cured 10, 20, 30 years out after HiCy. If you're not going to call that a cure, then none of us is cured of anything." But he and I really prefer to call HiCy a "potential" cure, because, "If you use the word 'cure,' people think everyone is cured, though 40-50 percent may not be."

Despite his caution in stating the case for HiCy as a total cure, evidence is clear that patients treated with HiCy must be reimmunized with all the childhood vaccines, starting a year after treatment. They react as if they have naïve immune systems.

"Rebooting the immune system" as an analogy for HiCy treatment was coined by Hopkins neurologist Daniel Drachman. He emphasizes that just as rebooting a computer doesn't wipe out all of its memory, for most people HiCy doesn't wipe out the entire mature immune system.

Judging from his work with myasthenia gravis, "What we're doing is setting back the immune thermostat to a lower level, setting the clock back," so patients previously refractory to standard treatment are treatable. "They're not cured in the sense that they're better forever," Drachman explains. "Some myasthenics are in good shape off of medicine for 10 years, then bingo, it's back."

“Buying time” by rebooting rather than curing forever is an explanation that also makes sense to Noel Rose, director of the Johns Hopkins Autoimmune Disease Research Center, since the immune system that’s reconstituted starts with the same stem cell progenitors as the original. “MS doesn’t usually occur until age 25 or 40,” he points out. “Most patients are willing to buy 25 years.”

## LIKE STOMACH FLU WITH A GOAL

Richard Bauer was in his prime when MS robbed him of movement. He decided to fight back.

Richard Bauer was on his feet all day as a machine operator, and working nights at a local steakhouse, when the symptoms first started. “I felt like my feet were wrapped tightly, like I had on 10 or 12 pairs of socks,” he recalls. “Within months, numbness and tingling traveled up my trunk, then down my left arm. My feet got really heavy, as if I had lead weights in my shoes, and my coordination began to go.”

Bauer’s life descended into a nightmare round of appointments with different doctors at different hospitals before he was diagnosed with multiple sclerosis (MS). His own immune system was attacking his body, stripping the myelin coating from his central nervous system.

Soon he was in a wheelchair, had lost hearing on the left side, and was forced to move back in with his family. Six months out of work, his insurance ran out, “But my parents insisted I keep an appointment with Dr. [Doug] Kerr in June 2005,” he recalls.

Kerr told Bauer and his parents about a “very intense” treatment with high doses of cyclophosphamide (HiCy), which kills off disordered cells so a patient’s own stem cells can regenerate and reboot a properly-functioning immune system. He was conducting a study of HiCy’s effectiveness against MS.

“MS was taking my life. I had to attack it as aggressively as it attacked me,” says Bauer. “If there’s a chance to fix me,” I told Dr. Kerr, “then fix me.”

Before he could be accepted for the protocol, Bauer went through two months of testing to make sure his heart and lungs could survive it. To be sure he understood the treatment’s risks—even a risk of death—and was capable of making an informed decision, he also agreed to a psychiatric evaluation.

Bauer was admitted to Hopkins Hospital on September 27, 2005, for four consecutive days of HiCy infusion. He’s candid about what happened next: “I didn’t feel bad until the second or third day. That’s when I got really sick, like a stomach virus&hellip; Every time I went to the bathroom, I felt like I was on fire.”

He went home after the fourth day, but came back daily to have his blood counts checked and for vancomycin [antibiotic] infusions. “That was the worst! I was allergic to it. I had hives from the top of my head to the bottom of my toes. I felt like I was burning up, but I had to take it for seven days.”

Blood counts dropping to 0 were a good sign and a warning. That meant his old immune system had been destroyed, but that he was vulnerable to every passing germ. A week of a special growth hormone stimulated his stem cells to do their rebuilding, and after four weeks, things started to reverse.

“I started walking to the bottom of the street and back, at first with a cane, and it took a long time,” he says. Gradually the distance increased and the time decreased. “I went from one block to a half-mile to two miles.” Today, Bauer runs 2 1/2 miles a day.

Back for his 24-month follow-up in October, the 30-year-old was the picture of health. With a diamond stud in his left ear, he’s six feet tall, sports a shaved head, and wears fashionable rimless glasses.

The good news for Bauer is that his “attack” against MS appears to have worked. Kerr found no disease activity by any measure. “In terms of a cure,” he admits, “it’s probably too soon to know for sure. It’s possible that he will reactivate over time. But for now, we couldn’t have hoped for any more with him.”

Bauer was one of nine patients accepted into Kerr’s study (funded through a private donation). Seven in the group had a statistically significant reduction in disability and restoration of function. Bauer’s newfound good health inspired him to return to college for a second degree, and he exudes optimism and good humor. “The treatment certainly wasn’t pleasant,” he says, “but it was no worse than stomach flu, and at least it had a goal. Conventional drugs wouldn’t have done much for me other than prolonging the inevitable. If [HiCy] were 10 times worse, it would have been worth it.” Taken from:

<http://www.hopkinsmedicine.org/hmn/W08/feature1.cfm>  
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