

Wholly Hopkins: "HiCy" relieves MS symptoms

Contributed by Virginia Hughes
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Chris Young, a former computer help-desk technician living in Denver, woke up one morning in June 2004 barely able to move the right side of his body. He felt spasms in the muscles between his ribs and a painful squeezing in his torso. When he tried to walk, he had trouble lifting his right foot. "I was scared out of my mind," he recalls. A few days later, an MRI scan confirmed what Young already suspected from looking up his symptoms on the Internet: He had multiple sclerosis (MS), a chronic disease in which the body attacks its own nerve fibers. The day of the diagnosis was his 29th birthday.

As his symptoms worsened over the next few years, Young frequently visited Internet forums for MS patients. In October 2007, a forum member described a new clinical trial at Johns Hopkins: Researchers would be testing cyclophosphamide, a chemotherapy drug ordinarily used to treat cancer, on patients with severe MS symptoms. By now Young had tried every known MS drug and nothing had helped. "I was dropping like a rock at that point," Young says. "So I figured, what have I got to lose?" He called the clinical trial's sponsor, Hopkins neurologist Doug Kerr, and was accepted for the study. On March 13, he was wheeled into Johns Hopkins Hospital to begin four days of intense chemotherapy.

Hopkins neurologist Doug Kerr thought HiCy might "reboot" an MS patient's immune system, allowing nerve cells to repair themselves. "The idea was to get rid of the inflammation entirely, in one fell swoop. When the immune system comes back up, we hoped, it would begin to behave better." Before the treatment, Young's abysmal short-term memory had him trapped in a state of fuzziness similar, he says, to what students feel after pulling an all-nighter. His wife would make lists to help him remember even two or three items-and he would promptly forget where he put the lists. Five days after treatment, Young woke up in the middle of the night and "everything was crystal clear," he recalls. The fog had lifted. "It was the freshest nap I've ever had."

Within a week of treatment, he could stand in a bathtub without having to hang on to the walls. Three months after that, he was walking without a cane.

Researchers began testing low-dose, long-term cyclophosphamide treatments in the 1980s. But that approach came with serious side effects. "It took the edge off inflammation, but it also made patients much more susceptible to infection, and even tumors," explains Kerr.

He and Hopkins colleagues Richard Jones and Robert Brodsky had for years used high doses of cyclophosphamide, given over just a few days, on hundreds of patients with various autoimmune disorders such as aplastic anemia and lupus. In those patients, "HiCy" therapy reversed disease progression with minimal toxicity. Kerr thought HiCy might "reboot" an MS patient's immune system, allowing nerve cells to repair themselves. "The idea was to get rid of the inflammation entirely, in one fell swoop," Kerr says. "When the immune system comes back up, we hoped, it would begin to behave better."

They were right. Of the first nine patients they treated with a high dose of cyclophosphamide, seven had a reduction in disability after two years. The results were published in June in the Archives of Neurology. Twenty-nine patients, including Young, have now been enrolled in a second trial, with similar motor improvements and no adverse drug effects so far.

"In most therapies for MS, the goal is only to make the disease slow down a little bit. Here, people actually got better," says hematologist and oncologist Douglas Gladstone of Hematology Oncology Associates of Western Suffolk, in New York. Additional research by Gladstone, who served a fellowship at Hopkins in the late 1990s, has also shown the effectiveness of HiCy on 14 MS patients. "This potentially represents a new standard of care," he adds.

The next step for HiCy development will be a phase-3, blinded clinical trial at multiple centers, Kerr says. For those patients whose disease did not go completely quiet with HiCy therapy, his team is also working on combination drug therapies that could be used after HiCy to increase its effectiveness. "These results are quite encouraging, but we certainly need to go further," he says. "This is only the first generation of trials." Originally published: August 2008 Taken from: <http://www.jhu.edu/~jhumag/0908web/wholly.html#hicy>