Patients with relapsing-remitting multiple sclerosis (MS) who have not responded well to one of the standard treatments for the disease can take heart: A new study has shown that supplementing beta interferons with the high-dose steroid methylprednisolone reduces the rate of relapse.

Approximately 85 percent of people with MS are initially diagnosed with relapsing-remitting MS. These patients experience attacks (called relapses) of worsening neurologic function, followed by either partial or complete recovery periods (called remissions). Typical MS symptoms include tremor, pain, fatigue, and dizziness. Symptoms occur because MS damages the insulating material (“myelin”) around nerve cells in the central nervous system.

**COMBINED TREATMENT STUDY**

The standard medications for treating relapsing-remitting MS are the beta interferons—interferon beta-1a (Rebif, Avonex) or interferon beta-1b (Betaseron)—and glatiramer acetate (Copaxone), says Gary Birnbaum, M.D., director of the Multiple Sclerosis Treatment and Research Center at the Minneapolis Clinic of Neurology, Ltd. While success rates vary from almost complete disease remission to no response at all, Dr. Birnbaum says, “Most people will have a reasonable response to one or the other drug, with a change in the pattern of their disease.”

Both classes of drugs—the beta-interferons and glatiramer acetate—work by modulating the immune system, says Dr. Birnbaum. The exact mechanisms of action are not completely known. But the end results are twofold: less infiltration of the central nervous system by immune cells capable of destroying myelin; and a change in the pattern of immune response to myelin, from a destructive to a protective one.

Steroids, in contrast, are general immune suppressants. They reduce inflammation throughout the body. Short-term use of steroids in people with MS reduces the duration of acute attacks and may promote healing, while their long-term use supplements the immune-modulating effects of the disease-modifying drugs. In some individuals, this results in better control of their MS.

“The usual approach for someone who doesn’t respond to a drug is to change to a different one,” Dr. Birnbaum says. For example, someone might be switched from one of the interferons to glatiramer acetate. If the person still doesn’t respond well, the neurologist might supplement the first disease-modifying medication with another drug. High-dose methylprednisolone, administered in single monthly pulses, is frequently used for this purpose, he says.

Hence the three-year study by Mads Ravnborg, M.D., of the Danish Multiple Sclerosis Research Center at Copenhagen University Hospital in Denmark and supported by Biogen Idec., which makes interferon beta-1a. The study examined the combined effect of methylprednisolone and interferon beta-1a on 341 people with relapsing-remitting MS. Half of the participants received 500 mg of oral methylprednisolone in monthly “pulses,” which means three doses over three days, in addition to regular weekly injections of the drug interferon beta-1a. The other
half received only interferon beta-1a and a placebo.

Prior to the study, participants had not received a disease-modifying drug like beta interferon. The average duration of disease among participants was three years.

**LOWER RELAPSE RATE**

The research team concluded that taking both methylprednisolone and interferon beta-1a reduced the rate of relapses—times when the disease is active—by 38 percent compared to standard treatment of the interferon drug alone. Patients on both drugs also improved on several tests that assessed leg functions, walking, arm-and-hand function, and cognitive function, while those on only interferon beta-1a saw their scores slightly decrease. The lesions in the brain that are a sign of disease activity were measured at the beginning and end of the study. For patients receiving both drugs, the lesions stayed the same size or shrunk, but for those taking only interferon beta-1a, the lesions grew.

“These results indicate that these two drugs may have a synergy when taken together and provide a more beneficial effect on disease activity,” says lead author Dr. Ravenborg. “This is a promising finding, as the benefit from interferon is only moderate and not everyone responds fully to the treatment. Anything we can do to boost those results is positive.”

“The concept of supplementing standard therapy with another immune-modulating therapy is not novel. What is important is that this study provides support for the efficacy of this approach,” Dr. Birnbaum notes.

Both steroids and beta interferons can cause significant adverse effects. Long-term use of steroids can cause cataracts, high blood pressure, weight gain, diabetes mellitus, and aseptic necrosis (in which parts of bone fail to get blood and die). Side effects of beta interferons can include flu-like symptoms, fatigue, and liver and thyroid changes.

Adding more drugs to a patient’s regimen typically increases the risks of side effects. But, says Dr. Birnbaum, “To the best of my knowledge, addition of monthly pulses of steroids does not alter the side-effect profile of the beta interferons and vice versa.” In the study, complications such as thinning bones, hair loss, and increased infections from the monthly steroid treatment were rare. Side effects in the study included heartburn, increased heart rate, and difficulty sleeping, but these symptoms were well controlled with medication, Dr. Ravenborg says.

Currently, the Food and Drug Administration does not approve the use of steroids as long-term therapy for MS. And experts warn that long-term, monthly courses of steroids could lead to serious complications. According to Dr. Birnbaum, single monthly pulses of high dose steroids can be continued for the long term with careful monitoring. But because of the potential for side effects, he adds, the combination treatment “should be reserved for those individuals who have not responded sufficiently to either one of the beta interferons or to glatiramer acetate, or were unable to tolerate these drugs.” —Elizabeth Stump
OUR KIND OF GUY

Stephen Allen

Stephen Allen, 24, is on a mission to prove to the world—the whole world—that despite his epilepsy, he can lead an active and fulfilling life. The founder of the Seize the World Foundation is spreading awareness of epilepsy and raising donations to fund research for a cure by biking all the way around the globe.

Allen's Web site documents his journey—visit the ongoing blog of his experiences at seizetheworld.com—which began in Telluride, CO, and progressed to Charleston, SC. From there he flew by plane to Portugal, and biked through France, Spain, and Italy along the Mediterranean coast. Currently he is in Turkey, and will eventually head to Egypt, India, China, and Japan. Allen will fly from Japan to Seattle and then finish the tour when he reaches his home in Telluride.

“His effort is almost superhuman and is truly inspiring,” says Seize the World Foundation volunteer Ian McKittrick. “Seize the World’s mission to fund epilepsy research can only be accomplished if Stephen’s story is heard and felt around the world. We hope Stephen’s journey will inspire individuals with epilepsy to achieve their own life goals and to seek more active lifestyles.”

Allen, who has had epilepsy since he was 15, planned the tour for a year prior to starting. Along the way, Allen has given talks at libraries, bookstores, and even epilepsy research centers. After recovering from a seizure upon his arrival in Lisbon, Allen forged ahead, greeted by cheers when he arrived at his next destination. Although he has used the train to get around occasionally, most of his journey has been by bike, at a 10 mph pace.

He has also endured brutally cold weather and the onslaughts of traffic. While biking from Seville toward Valencia, Allen says, it was so cold that he could barely pedal. But, he says, “The experience of being a cyclist on Spain’s back roads during such conditions, riding through the olive country, was beautiful.”

“Yes, I have epilepsy, but I also have memories of amazing freedom,” Allen says. “There will always be challenges in life, but I know that no matter where I go, there will also be great people along the way.” —Elizabeth Stump

NEUROLOGY NEWS

Restless Legs Syndrome

According to the RLS Foundation, one in ten American adults suffer from restless legs syndrome (RLS), a neurological condition characterized by the irresistible impulse (often described as a “creeping” or “itching” feeling) to move one's legs. Symptoms are usually more pronounced at night and interfere with sleep.

The only drugs approved for RLS treatment are “dopamine agonists” (which activate dopamine receptors when the body cannot), including ropinirole (Requip) and pramipexole (Mirapex). A new study, however, has shown the anti-convulsant pregabalin (lyrica) to also be effective in mitigating symptoms of the condition.

“Patients with RLS improved significantly more under treatment of pregabalin than under placebo,” says Diego Garcia-Borreguerro, M.D., director of the Sleep Research Institute in Madrid, Spain.

In fact, Dr. Garcia-Borreguerro’s double-blind, placebo-controlled study of 58 patients showed pregabalin to be an effective means of both reducing RLS symptoms and improving quality of sleep. “After 12 weeks of treatment, we were able to reduce virtually all RLS symptoms in 63 percent of the patients,” Dr. Garcia-Borreguerro says, “and their sleep improved significantly.”

While participants in the study did suffer side effects from pregabalin (including unsteadiness or dizziness), Dr. Garcia-Borreguerro says the drug was generally “well-tolerated.”

“We still need to do a large, multicenter, well-controlled study that confirms these,” says Rajesh Pahwa, M.D., director of the Parkinson Disease and Movement Disorder Center at the University of Kansas Medical Center. “But it’s good to know there’s another class of drugs that may help.” —Todd Farley
**QUICK TIPS**

**What to Tell Your Neurologist**

How can you get the best care? Start by telling your neurologist what he really wants to know. We talked with Gary Gronseth, M.D., vice chairman of the department of neurology at the University of Kansas Medical Center. Dr. Gronseth often writes guidelines for neurologists on how best to evaluate and treat neurological problems. Here’s what he wants you to discuss:

- **YOUR SYMPTOMS:** “Tell me the story of your symptoms, not what other people have told you about your symptoms,” Dr. Gronseth says. “Be as specific as possible and concentrate on when the symptoms started and how they progressed.”

- **OTHER MEDICAL CONDITIONS:** “It’s really important to know the patient’s other medical conditions, allergies, and idiosyncratic reactions to medications,” he says. “That way, if there are several treatment options, the neurologist can pick the one that best fits the patient and will do no harm.”

- **MEDICATIONS:** “Don’t forget over-the-counter (OTC) drugs, vitamins, supplements, and herbs.”

- **ILlicit DRUGS:** “People are understandably reluctant to talk about this, but you should, because it may be related to your problem. For example, cocaine or amphetamines cause strokes, and some OTC medications—like diphenhydramine (Benadryl)—can cause memory problems and confusion.

- **FAMILY HISTORY, INCLUDING GAPS:** “Some people lose contact with relatives and may not want to admit it. But a gap in family history will be very useful for the neurologist in excluding or continuing to consider the cause of your symptoms.”

- **WHAT YOU WANT OUT OF TREATMENT:** “The neurologist needs to understand the patient’s values. For example, we often put stroke survivors on blood-thinners. But if the patient has had a bleeding complication in the past and is concerned about it happening again, he should bring it up. Encourage the physician to have a risk-benefit discussion where you can ask ‘Gee, doc, is this really going to be worth it for me?’”

**TIP US OFF!** Do you have a tip for managing neurological illness, making the most of doctor visits, or saving money on health care? Send it to neurologynow@lwtny.com or mail it to: Neurology Now, 333 Seventh Ave., 19th floor, New York, NY 10001.

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**READING ROOM**

**Still Alice**

In Lisa Genova’s debut novel, Still Alice (Pocket Books, 2009), 50-year-old Alice Howland is at the pinnacle of her career—enjoying acclaim as a distinguished professor of psychology at Harvard and savoring the accomplishments of her grown children and Harvard professor husband—when she begins to experience moments of confusion and forgetfulness. The episodes increase and intensify until Alice can no longer dismiss them as signs of routine stress and aging. After Alice takes a genetic test, her neurologist delivers the devastating diagnosis: She is positive for a mutation linked with early-onset Alzheimer’s disease. When Alzheimer’s affects someone before the age of 65, it is known as early-onset. According to the Alzheimer’s Association, there are approximately 5 million people living with Alzheimer’s disease in the United States. And 500,000 of them—or 10 percent—are under the age of 65. While earlier cases have been documented, early-onset Alzheimer’s typically affects people in their 50s.

Each chapter chronicles a consecutive month in Alice’s life. Genova, who holds a Ph.D. in neuroscience from Harvard, details the disease’s progression over a two-year span with sensitivity and scholarship. We observe Alice as she explores her treatment options, participates in a clinical trial of a promising drug, and attempts to cope with the unpredictable nature of her condition. Written from Alice’s point of view, readers are able to experience her frustrations, confusion, and terror first-hand.

Genova’s novel is also an inquiry into personal identity. As her career and memories fall apart, Alice is forced to question who she is. “Is the part of my brain that’s responsible for my unique ‘me-ness’ vulnerable to this disease?” she asks. “Or is my identity something that transcends neurons, proteins, and defective molecules of DNA? Is my soul and spirit immune to the ravages of Alzheimer’s?” Genova affirms that the person who remains—in spite of her diminishments—is still valuable and often vibrant; and she shows how personal identity is derived in part from the love and memories of those around us.

The novel’s success today belies the challenges it faced finding a publisher. Passed over by several publishing houses, an endorsement from The National Alzheimer’s Association gave Genova the conviction to self-publish. It went on to win the 2008 Bronte Prize for best love story in North America and was then picked up by Simon & Schuster’s Pocket Books. Upon its release in January 2009, it debuted at #5 on The New York Times Bestseller List. —Sean Chung