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'HiCy' drug regimen reverses ms symptoms in selected patients

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A short-term, very-high dose regimen of the immune-suppressing drug cyclophosphamide seems to slow progression of multiple sclerosis (MS) in most of a small group of patients studied and may even restore neurological function lost to the disease, Johns Hopkins researchers report. The findings in nine people, most of whom had failed all other treatments, suggest new ways to treat a disease that tends to progress relentlessly.

"We didn't expect such a dramatic return of function," says Douglas Kerr, M.D., Ph.D, associate professor of neurology at the Johns Hopkins University School of Medicine. "Although we're very early in the game, we think this approach could be the linchpin of a significant advance for MS treatment."

Researchers have used the so called HiCy treatments with some success at Johns Hopkins for a variety of other immune system disorders, including aplastic anemia, lupus and myasthenia gravis.

Cyclophosphamide kills immune-system cells but spares the bone marrow stem cells that make them. The usual method of delivering it in pulsed, small doses, however, can cause the drug to build up to toxic concentrations in patients' bodies, causing a variety of side effects, including a greatly increased risk of infection.

Seeking an alternative way to use the drug, Kerr and his colleagues reasoned that HiCy might clear out the majority of a patient's immune

system in one fell swoop, then allow it to "reboot," giving nerve cells a fresh start and an opportunity to repair themselves. In the current study, nine MS patients got a total single infusion of 200 milligrams per kilogram of cyclophosphamide intravenously over four days, a dose several times higher than that given in pulsed regimens but significantly lower than the total amount usually given patients over time.

Before treatment, Kerr says, the study participants were "the worst of the worst" among MS patients. Eight of the nine patients had failed conventional MS treatments, and several of them were wheelchair-bound.

Reporting in the June 9 *Archives of Neurology*, the Johns Hopkins team said the disease appeared to reverse course for seven of the nine patients over two years following treatments. Overall, the patients, men and women ranging in age from 20 to 47 at the beginning of the study, experienced a 40 percent reduction in scores of a standard test that measures disability. They also had an overall 87 percent improvement in scores on a composite test that measures physical and mental function.

MS, which affects approximately 400,000 people - predominantly women - in the United States, is believed to occur when the body's immune system attacks the insulating sheath that coats nerve cells, causing it to degenerate. Consequently, electrical signals that the cells use to communicate with the rest of the body become progressively weaker, leading to symptoms that include numbness, tingling, cognitive problems and sometimes paralysis.

Researchers have identified four different subtypes of MS, and each is thought to be caused by a different autoimmune process. As a result, developing a treatment that effectively targets all types of MS has been challenging, says Kerr.

Kerr cautions that the "reboot" phenomenon didn't work in all the patients. Two years after treatment, MRI images showed that the disease had reactivated in about half the study participants, suggesting that their renewed ability may not be permanent.

Kerr's colleague Adam Kaplin, M.D., Ph.D., assistant professor of psychiatry and neurology at the Johns Hopkins School of Medicine, is leading efforts to improve HiCy therapy with a blood test in development that could predict which patients would benefit the most from HiCy treatment. Also, since immune cells that regrow after HiCy treatment may contain the same defect that leads to MS, Kaplin and his colleagues are working on a way to regrow only healthy immune cells.

Source: Johns Hopkins Medical Institutions