DNA vaccine against multiple sclerosis appears safe, potentially beneficial

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A newly developed DNA vaccine appears safe and may produce beneficial changes in the brains and immune systems of individuals with multiple sclerosis, according to an article posted online today that will appear in the October 2007 print issue of *Archives of Neurology*, one of the JAMA/Archives journals.

In patients with multiple sclerosis (MS), the immune system attacks the myelin sheaths that protect nerve cells in the brain and spinal cord, according to background information in the article. The nerve cell's axon, which transmits messages to other neurons, is eventually destroyed. The cause of MS is unknown, but evidence points to the involvement of immune cells and antibodies that recognize and attack specific substances in the myelin, such as myelin basic protein. Certain cytokines, small proteins produced by cells that trigger inflammation, also may play a role.

Amit Bar-Or, M.D., of the Montreal Neurological Institute and colleagues tested a DNA vaccine, BHT-3009, that encodes a full-length human myelin basic protein. Between 2004 and 2006, the researchers administered the vaccine to 30 patients with relapsing-remitting MS [characterized by symptomatic periods and periods of remission] or secondary progressive MS [when symptoms progressively worsen, but there still may be periods of remission]. After one, three, five and nine weeks, participants received intramuscular injections of placebo or BHT-3009 (in doses of .5 milligrams, 1.5 milligrams or 3 milligrams), with or without 80-milligram pills of atorvastatin calcium, a lipid-

lowering drug previously shown to be effective in autoimmune conditions. After 13 weeks, participants who initially received placebo received four injections of BHT-3009.

Magnetic resonance imaging (MRI) and other safety evaluations were performed at the beginning of the study, and again after five, nine, 13, 26, 38 and 50 weeks. “BHT-3009 was safe and well tolerated, provided favorable trends on brain MRI and produced beneficial antigen-specific immune changes,” the authors write. These changes included a reduction in the number of cytokine-producing CD4+ T cells (a type of white blood cell) specifically targeting myelin proteins. This reduction was found in the blood as well as in the cerebrospinal fluid of three patients who voluntarily underwent lumbar puncture after completing the course of BHT-3009. Atorvastatin did not appear to provide additional benefit.

“There were no increases in clinical relapses, disability, drug-associated laboratory abnormalities, adverse events or the number and volume of contrast-enhancing [visible on MRI] lesions on brain MRI with BHT-3009 treatment compared with placebo,” the authors write. “In fact, there was a trend toward a decrease in the number and volume of contrast-enhancing lesions in the brain in patients treated with BHT-3009 compared with placebo.”

Source: JAMA and Archives Journals