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TREATMENT OF MULTIPLE SCLEROSIS WITH GAMMA INTERFERON: EXACERBATIONS ASSOCIATED WITH ACTIVATION OF THE IMMUNE SYSTEM

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We treated 18 clinically definite relapsing-remitting MS patients with recombinant gamma interferon in a pilot study designed to evaluate toxicity and dosage. Patients received low (1 μg), intermediate (30 μg), or high (1,000 μg) doses of interferon by intravenous infusion twice a week for 4 weeks. Serum levels of gamma interferon were proportional to dose and no interferon was detected in CSF. Seven of the 18 patients had exacerbations during treatment, a significant increase compared with the prestudy exacerbation rate ($p < 0.01$). Exacerbations occurred in all three dosage groups and were not precipitated by fever or other dose-dependent side effects. There were significant increases in circulating monocytes bearing class II (HLA-DR) surface antigen, in the proliferative responses of peripheral blood leukocytes, and in natural killer cell activity. These results show that systemic administration of gamma interferon has pronounced effects on cellular immunity in MS and on disease activity within the CNS, suggesting that the attacks induced during treatment were immunologically mediated. Gamma interferon is unsuitable for use as a therapeutic agent in MS. Agents that specifically inhibit gamma interferon production or counteract its effects on immune cells should be investigated as candidates for experimental therapy.

Comment from Richard M. Ransohoff, MD, Associate Editor: *A very important and startling clinical trial failure, considered counterintuitive at the time, but which later illuminated MS pathogenesis.*