The underlying etiology and pathogenesis of Gulf War veterans’ illnesses continue to be under intense investigation. Reports have suggested the basis for these illnesses may be an altered immune system, but compelling evidence is lacking. We sought to determine whether in vitro immune responses were abnormal in symptomatic Gulf War veterans relative to matched controls. A randomized case-control study was conducted by blinded comparison of laboratory measures of in vitro immune responses in blood samples obtained from veterans in an outpatient facility of a Veterans Affairs medical center. Symptomatic Gulf War veterans with otherwise undefined illnesses (52 symptomatic subjects), asymptomatic Gulf War veterans (31 asymptomatic controls), and veterans who had applied for disability compensation and had not participated in the Gulf War (21 disability controls) represented the volunteer sample. In vitro cellular and humoral immune responses were measured to detect functional abnormalities in antigen presenting cells (autologous mixed leukocyte reactions and expression of interleukin (IL)-1beta, IL-6, IL-10, and tumor necrosis factor-alpha); T cells (lymphocyte proliferation using the polyclonal T-cell activators phytohemagglutinin and Concanavalin A; primary immune responses in allogeneic mixed leukocyte reactions; secondary immune response using the recall antigens
tetanus toxoid, Candida albicans, and anthrax vaccine; and soluble IL-2 receptor expression); type-1 T-helper cells (gamma interferon expression); type-2 T-helper cells (IL-4 and IL-10 expression); and B cells (polyclonal B-cell activator pokeweed mitogen-induced immunoglobulin production). In general, immune response measures did not differ significantly between groups. Heightened responses observed in the disability control group (sporadically greater responses to one mitogen and two antigens) and the Gulf War participation control group (greater recall responses to anthrax vaccine) did not suggest impaired immune cell function in symptomatic veterans when compared with controls. We conclude that in vitro immunological responses are not abnormal in symptomatic Gulf War veterans.