A Research Campaign to Understand the Gulf War Syndrome

I will describe our 8-year research effort to understand the epidemic of neurologic symptoms that affected an estimated 100,000 of the 700,000 U.S., British, Canadian and Australian troops who served in the 1991 Persian Gulf War. Our initial studies focused on 249 members of a Reserve Naval Mobile Construction Battalion, or Seabees. In that work, we made four important observations. First, exploratory factor analysis of symptoms identified a single Gulf War illness with three variants. The factor structure was recently replicated in a new Gulf War veteran sample with structural equation modeling. Second, a sample of those with the illness have more abnormal brain function by objective tests than a sample of well veterans, suggesting a brain injury or illness. Third, the sick veterans were 4 to 32 times more likely than well veterans to report exposure to combinations of certain chemicals in the war, specifically low level sarin nerve gas, side effects from pyridostigmine anti-nerve gas medication, highly concentrated government-issue DEET insect repellent, and pesticides in flea collars. And fourth, in collaboration with researchers at Duke and Kansas State universities and the EPA, we experimentally produced brain and nerve damage in hens with combinations of some of these same chemicals, not previously thought to be neurotoxic. A research group in India led by K. Husain, has extended these findings by demonstrating neurological damage from low-level sarin nerve agent in two animal species. Survivors of the Tokyo subway sarin attack report similar chronic symptoms and neurologic findings. A second set of case-control studies made four additional observations. First, we identified a genetic polymorphism in the PON1 gene that appears to have predisposed soldiers to getting the Gulf War syndrome and appears to link the illness with low-level sarin nerve gas exposure. Second, we used a relatively new brain scanning approach called Magnetic Resonance Spectroscopy (MRS) to demonstrate abnormal brain cell metabolism in deep brain structures in the ill veterans compared with well controls. Third, we found abnormal increases in production of the brain neurotransmitter dopamine in those veterans with the worst brain cell damage measured by the MRS scans. In independent studies of ill Gulf War veterans and well controls, researchers in the U.K. have replicated the PON1 genetic association, and researchers at UC San Francisco have replicated the MRS evidence of a brain cell metabolic abnormality. In collaboration with Research Triangle Institute we will soon begin a national random sample survey to attempt to confirm this disease model. In parallel we are developing more advanced brain imaging capabilities, such as functional MRI, to attempt to demonstrate the location and nature of the brain dysfunction more definitively.