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Editorial

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On the Need for Epidemiologic Studies of Gulf War Illness among African-American Veterans

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About 16 percent of the nearly 700,000 military personnel who served in the 1991Gulf War (GW) were African American men and women (Khan, K.H., et al; 2000). Multiple studies have looked at rates of Gulf War Illness (GWI) among Gulf War Veterans, and several have assessed medical and psychiatric issues that differ by race in this population. However, few studies have reported race-specific rates of GWI and no studies have provided detailed race-specific information about symptoms.

Results from two Kansas studies (Steele, L., 2000; Steele, L., et al. 2012) suggest that GWI is more common in African American GW Veterans than their white counter parts. However, in the 27years since the war, few studies have evaluated GWI and other medical conditions specifically as they affect African American Veterans of the1991 GW. In 1998, Steele conducted a population-based survey of 1,538 Veterans who served in the 1991 GW and 482 Veterans who served elsewhere. About 15% of GW Veterans and 12% of non-GW Veterans were black. The unadjusted odds ratio (OR) for GWI was 1.93 for black versus white race (95% confidence interval [CI] = 1.32, 2.83). After adjustment for sex, income, education, branch of service, rank, location in theater, and time period in theater, the OR for black race was 1.23 (95% CI = 0.81, 1.87). Steele et al. (2012) conducted a case-control study of GWI embedded within a population-based sample of Veterans in the greater Kansas City metropolitan area. Potential participants were excluded if they reported being diagnosed by a physician with chronic medical conditions that might account for their symptoms or had persistent health problems due to chronic infection or serious injury. Veterans were also excluded if they reported being diagnosed with serious psychiatric conditions or if they had been hospitalized since the GW for alcohol or drug dependence, depression, or post-traumatic stress disorder. Among the sample of 144 cases of GWI and 160 controls the unadjusted OR for black race was 3.43 (95% CI 1.40, 8.44).

Taken overall, surprisingly little research has been conducted to follow up on findings from studies suggesting that African American veterans of the GW had excess rates of GWI (Steele, L., 2000; Steele, L., et al. 2012). In the majority of published epidemiologic studies of the health of GW Veterans race was controlled for in the analysis and no race-specific results were provided (Khan, K.H., et al. 1996; 2000; 2001; Spemcer, et al. 2001; Gray, et al. 2002; Camey, et al. 2003; Smith, et al. 2007; Vogt, et al. 2007; Young, et al. 2010; Iannacchione, et al. 2011; Smith, et al. 2013; Dursa, et al. 2016; Barth, et al. 2016; Porter, et al. 2018). In some studies, race was not addressed in the analysis or the sample did not include African American Veterans (Macfarlane, et al. 2003; 2005).

The results of clinical studies of GWI support the biologic plausibility of an association with race. Some studies have found an association between paraoxonase (PON1) and risk of GWI (Golomb, 2008). Studies have found that excess illness in GW Veterans can be explained in part by exposure of GW Veterans to organophosphate and carbamate acetylcholinesterase inhibitors (AChEis), including pyridostigmine bromide (PB), organophosphate pesticides, and nerve agents (Golomb, 2008; White, et al. 2016; Coughlin, 2017). Epidemiologic studies have shown a link between AChEi exposure and chronic symptoms in GW Veterans. The link is supported by a relation between avidity of AChEi clearance and illness, based on genotypes, concentrations, and activity levels of enzymes that detoxify AchEis (Golomb, 2008). African Americans have higher paraoxonase levels than whites, consistent with African Americans having a lower proportion of the functional genotype QQ (QQ 15%, QR 34%, RR 44%, 7% indeterminate), than whites (Davis, et al. 2009).

Studies of the role of humoral immunity in GWI have examined the frequency of human leukocyte antigen (HLA) alleles (O'Bryan, et al. 2003; Georgopoulos, et al. 2016). HLA Class II proteins are located in the Major Histocompatibility Complex (MHC) of chromomose 6 and are expressed on all nu-

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cleated cells. They play a role in immune recognition by presenting peptides from exogenous proteins to CD4+ helper T cells (Meuer, et al. 1982). Results of clinical research studies are consistent with the hypothesis that environmental triggers (e.g., organophosphate pesticides, sarin or cyclosarin nerve agents, and pyridostigmine bromide medication) contributed to the development of GWI in genetically susceptible Veterans who had lower frequencies of HLA alleles that conferred protection. Studies have identified extensive differences in HLA alleles between African Americans and whites (Allele frequencies, 2018).

Epidemiologic studies are needed to examine the prevalence and patterns of GWI symptoms and diagnosed medical conditions among African American men and women who served during the GW. The studies should provide a comprehensive picture of the health of African American GW Veterans. This includes assessment of current health status, changes in health symptoms and conditions overtime, and possible differences in health outcomes associated with specific experiences and exposures during the war. Studies should allow for an assessment of GWI symptom atterns that may be specific to African American Veterans and a determination of diagnosed medical conditions among African American Veterans. Black-white differences in GWI should be examined to determine whether GWI manifests differently in African American men and women. Epidemiologic studies are needed to improve our understanding of GWI in African American Veterans who served in the1991 GW, and to lay the groundwork for future research aimed at a short-term or longer-term improvement in clinical treatment of African American Veterans with GWI, and the definition and diagnosis of GWI in African American Veterans. Results of epidemiologic research can lay the groundwork for clinical and laboratory studies aimed at clarifying genetic factors predisposing individuals to GWI, identifying biomarkers that underlie symptom clusters among African American GW Veterans, and developing diagnostic tests for GWI that are suitable for diverse Veteran populations.

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