

GULF WAR ILLNESS



IS REAL

AND IT CAN BE SERIOUS

Gulf War Illness (**GW**I) is a chronic multi-symptom health problem that affects ~1/3 of the ~700,000 US veterans deployed to the Persian Gulf War (1990-1991).

DIAGNOSIS

CDC [24] and Kansas [25] criteria are used to establish diagnosis. Both require deployment to the Gulf theater (8/90 to 8/91) and persistent symptoms (>6 months). Symptom requirements:

- CDC: One or more symptom in at least two of the three categories of fatigue, mood-cognitive, musculo-skeletal.
- Kansas: Symptoms (either multiple within the category or of at least moderate severity) in ≥ 3 of 6 domains of neurological-cognitive-mood, pain, fatigue/sleep, respiratory, skin and gastrointestinal.

CAUSES

Gulf War veterans had many new, unique, and excessive exposures. These include:

- Pyridostigmine bromide pills* 
- Pesticides* 
- Nerve gas* 
- New, unique & greater number of vaccines*
- Oil fires 
- Depleted uranium 
- Permethrin-impregnated uniforms

*These have been tied to GWI [1-4].

ASSOCIATED CONDITIONS

Gulf War veterans are at *increased risk* for:

- ALS (early years only) [5]
- Hypertension [6]
- Heart disease [7]
- Infection [7]
- Sleep apnea [8]
- Overlap conditions (CFS [6,9], MCS [6], fibromyalgia [9], IBS [6])

OBJECTIVE MARKERS- ALTERED IN GWI

- ↓ Mitochondrial function/bioenergetics [10,11]
- ↑ Inflammation (mild), neuroinflammation [12,13]
- ↑ Coagulation activation [13]
- Altered lipids [14,15]
- Altered hormones [16,17]
- ↑ Autoantibodies [18]
- ↑ Autonomic dysfunction [19,20]
- ↓ Natural killer cells (#, activity) [18,21]
- ↓ Brain gray matter; white matter changes [22,23]



Provider Attitudes Matter

- Best vs. worst healthcare encounters involved veterans feeling honored, validated, perceiving empathy, effort to help, and provider knowledgeable about GWI.
- Worst encounters *often* involve providers disbelieving veterans – suggesting they were malingering, symptoms were in their head, or attributing symptoms to stress or age.
- Providers implying GWI is malingering, is in veterans' heads, or is not tied to Gulf exposures strongly predicted veterans mistrust of providers, which in turn predicted nonadherence to doctor recommendations and nonreturn for care (all $p < 0.0001$) – threatening care not only for veterans' Gulf War illness, but for their other health conditions..
- You can make a difference!



References

1. Golomb BA. Acetylcholinesterase inhibitors and Gulf War illnesses. *Proc Natl Acad Sci* 2008;105(11):4295-300.
2. Steele L, et al. Association of deployment characteristics and exposures with persistent ill health among 1990-1991 Gulf War veterans in the VA Million Veteran Program. *Environ Health*. 2024 Oct 25;23(1):92.
3. Schumm WR, et al. Self-reported changes in subjective health and anthrax vaccination as reported by over 900 Persian Gulf War era veterans. *Psychol Rep*. 2002 Apr;90(2):639-53.
4. Cherry N., et al. Health and exposures of United Kingdom Gulf war veterans. Part II: The relation of health to exposure. *Occup Environ Med* 2001;58(5):299-306.
5. Haley RW. Excess incidence of ALS in young Gulf War veterans. *Neurology* 2003;61(6):750-6..
6. Gray GC, et al. Self-reported symptoms and medical conditions among 11,868 Gulf War-era veterans: the Seabee Health Study. *Am J Epidemiol* 2002;155(11):1033-44. DOI: 10.1093/aje/k155.11.1033.
7. Simmons R, et al. Self-reported ill health in male UK Gulf War veterans: a retrospective cohort study. *BMC Public Health* 2004;4:27.
8. Amin MM, et al. Inspiratory airflow dynamics during sleep in veterans with Gulf War illness: a controlled study. *Sleep Breath* 2011;15(3):333-9.
9. Eisen SA, et al. Gulf War veterans' health: medical evaluation of a U.S. cohort. *Ann Intern Med* 2005;142(11):881-90.
10. Golomb, et al. Mitochondrial impairment but not peripheral inflammation predicts greater Gulf War illness severity. *Sci Rep* **13**, 10739 (2023).
11. Golomb BA, et al. Bioenergetic impairment in Gulf War illness assessed via 31P-MRS. *Sci Rep*. 2024 Mar 28;14(1):7418.
12. Alshelhi Z., et al. In-vivo imaging of neuroinflammation in veterans with Gulf War illness. *Brain Behav Immun*. 2020;87:498-507.
13. Johnson GJ, et al. Elevated platelet count, C-reactive protein and thromboxane analog-induced platelet aggregation in patients with Gulf War veterans' illnesses: evidence of a chronic inflammatory state? *Blood Coagul Fibrinolysis* 2013;24(7):736-41.
14. Naviaux RK., et al. Metabolic features of Gulf War illness. *PLoS One* 2019;14(7):e0219531.
15. Oberlin S., et al. Sex-specific differences in plasma lipid profiles are associated with Gulf War Illness. *J Transl Med*. 2022;20(1):73.
16. Golier JA, et al. Enhanced cortisol suppression to dexamethasone associated with Gulf War deployment. *Psychoneuroendocrinology*. 2006;31(10):1181-9.
17. Golier JA, et al. Twenty-four hour plasma cortisol and adrenocorticotrophic hormone in Gulf War veterans: relationships to posttraumatic stress disorder and health symptoms. *Biol Psychiatry*. 2007;62(10):1175-8.
18. Vojdani A, Thrasher JD. Cellular and humoral immune abnormalities in Gulf War veterans. *Environ Health Perspect* 2004;112(8):840-6.
19. Haley RW, et al. Blunted circadian variation in autonomic regulation of sinus node function in veterans with Gulf War syndrome. *American Journal of Medicine*. 2004;117(7):469-78.
20. Haley RW, , et al. Cholinergic autonomic dysfunction in veterans with Gulf War illness: confirmation in a population-based sample. *JAMA Neurol*. 2013;70(2):191-200.
21. Zhang Q., et al. Changes in immune parameters seen in Gulf War veterans but not in civilians with chronic fatigue syndrome. *Clin Diagn Lab Immunol* 1999;6(1):6-13.
22. Heaton KJ, Palumbo CL, Proctor SP, Killiany RJ, Yurgelun-Todd DA, White RF. Quantitative magnetic resonance brain imaging in US army veterans of the 1991 Gulf War potentially exposed to sarin and cyclosarin. *Neurotoxicology* 2007;28(4):761-9.
23. Van Riper SM, et al. Cerebral white matter structure is disrupted in Gulf War Veterans with chronic musculoskeletal pain. *Pain*. 2017;158(12):2364-75.
24. Fukuda, K. et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *J. Am. Med. Assoc*. 280, 981-988 (1998).
25. Steele, L. Prevalence and patterns of Gulf War illness in Kansas veterans: Association of symptoms with characteristics of person, place, and time of military service. *Am. J. Epidemiol*. 152, 992-1002 (2000).