Gulf War Illness (GWI): Need for an ICD-10-CM Diagnostic Code

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On behalf of the consortium of GWI clinicians, researchers, and patient advocates

Overview

- Gulf War had unprecedented exposures
- Many who served became ill
- GWI is tied causally to drugs/chemicals
- GWI is defined by symptoms
- Many objective markers are altered
- GWI has ↑ risk of comorbidities
- An ICD-10-CM code is needed!

The 1990-1991 Gulf War Had Unprecedented Exposures

- Not excessive stress: Ground war only 4 days, many never saw combat
- Many new, unique, excessive exposures[1,2], e.g.,:
  - Pyridostigmine Bromide (PB)[3,4]: Nerve agent protection pill
  - Pesticides[3,5,6]: E.g., organophosphates, Carbamates, Pyrethroids
  - Nerve Gas (Organophosphate)[3,7]: Sarin, Cyclosarin

Many Who Served Became Ill

- Fraction ill = ~1/3 (subtracting fraction ill in non-deployed):
- Consistent across multiple studies[1-5]

GWI Tied (Causally) to Drugs/Chemicals

- Example: Pyridostigmine Bromide (PB): nerve agent protection pill

1. Dose response[1,2]:

PB pill #	0	1-2	3-10	~22-42	~>42
% ill	16	23	32	42	75
					P<0.0001

2. Gene-environment interaction[3]:

BChE* Genetics

	Usual	Rare Allele
OR† for Illness with PB	2.7	40
(95% CI)	(1.62-4.44)	(3.58-447)

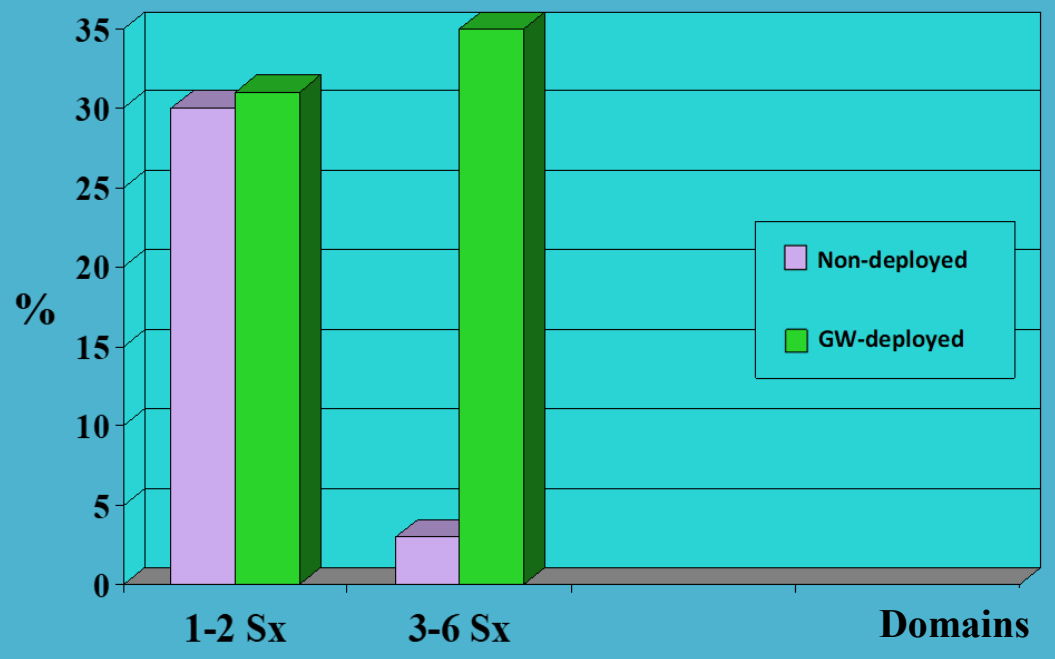
3. Meets Hill's Criteria for Causality[1]

*BChE = butyrylcholinesterase – detoxifies PB

†OR = odds ratio

GWI is Defined by Symptoms (and Deployment)

- GWI is defined by complex of symptoms that occur in domains that are highly consistent across Gulf War veteran populations and studies[1,2]



Y axis: % reporting this number of symptom domains

Kansas GWI criteria

Chronic symptoms (≥6 months*), either multiple or > mild, in at least 3 of 6 domains:

- Neurological
- Fatigue/sleep
- Respiratory
- Pain
- GI
- Skin

- Modified Kansas criteria for ICD: Exclusions required for research homogeneity include conditions that GWI increases risk of – not disqualifications clinically.

*Most with GWI have had symptoms persist for greater than 30 years

GWI: Many Objective Markers are Altered

- ⬇ Mitochondrial function/bioenergetics[1-3] (also GWI animal models)[4,5]
- △ Lipidomics, lipid products[6-8] (also GWI animal models)[9-11]
- ⬆ Inflammation (mild), coagulation[12-14]
- ⬆ Neuroinflammation[15] (also GWI animal models)[16,17]
- ⬆ Autoantibodies[18-20]
- ⬆ Autonomic dysfunction[21-23]
- △ Hormones[24-26]
- ⬇ Natural killer cells (number, activity)[18,27,28]
- Brain imaging: ⬇ gray matter; white matter changes[29-31]

GWI: Increased Risk of Comorbidities

- ALS (early years only)[1-3]
- Hypertension[4-9]
- Heart disease[7,10,11]
- Infection[10]
- Sleep apnea[12,13]
- "Overlap conditions": CFS[4,6,8,13-15], MCS[4,6,13,15,18,19], fibromyalgia[14,16,17], IBS[6,17]

ALS = amyotrophic lateral sclerosis; CFS = chronic fatigue syndrome;
MCS = multiple chemical sensitivity; IBS = irritable bowel syndrome

GWI is Not Captured in Other Diagnoses

- Not PTSD
  - Combat stress shows no independent association to GWI (in studies that control for other exposures)[1]
- Not TBI (traumatic brain injury)
- Not depression
  - Antidepressants among the worst treatments per many veterans' reports
- Not psychologically driven/psychiatric
  - Those without psychiatric symptoms have ~as much physical impairment as those with[2]

An ICD-10-CM Code is Needed!

- Federal research funds for GWI – 44 clinical studies, 9 patents, 277 papers – still no ICD-10-CM code
- An ICD-10-CM code is needed to aid:
  - Research
  - Epidemiological tracking
  - Clinicians:
    - No ICD-10-CM code = GWI doesn't exist
    - Wrong treatments, referrals
    - Diagnosis (code) points doctor to right literature – helps them help patients
  - Patients:
    - Terrible care experience for many[1]

Feb. 2023 RAC meeting: veterans again plead for GWI ICD-10-CM code

Recap

- Gulf War typified by heavy exposures: e.g., PB, pesticides, sarin
- ~1/3 became ill as a result: few improved[1-3]
- Chemicals (not stress) relate causally to illness
- GWI is defined by symptoms (and deployment)
- Many objective markers are altered
- Many comorbidities are increased
- An ICD-10-CM code is needed
  - No other ICD-10-CM code answers!

Submitting Consortium Highly Credentialed in GWI

- Consortium of GWI clinicians, researchers, patient advocates
- Directors of patient clinics focused on GWI
- 37 GWI DoD grants as PI
- 179 GWI publications (PubMed)
- 3 scientific directors of congressionally-charged Research Advisory Committee on GWI (RAC)
- 3 RAND reports
- Invited to testify for ~every NAS, NAM, IOM committee on GWI
- Testimony to Congress (times many) – also House of Lords (UK)
- Developed validated (Kansas) GWI diagnostic criteria
- Directors of GWI Biobank, GWI clinical trial consortium
- 2 heads of overall DoD GWI research program panel
- Chaired <u>many</u> individual research award review committees
- Members of VA GW Steering Committee (1st GWI research strategic plan)
- Clinical experience with countless affected veterans