

Genetic study confirms sarin nerve gas as cause of Gulf War illness

May 12 2022



Dr. Robert Haley, here reviewing brain scans of Gulf War veterans, has been studying the illness for 28 years. Credit: UT Southwestern Medical Center

For three decades, scientists have debated the underlying cause of Gulf War illness (GWI), a collection of unexplained and chronic symptoms affecting veterans of the Persian Gulf War. Now researchers led by Robert Haley, M.D., Professor of Internal Medicine and Director of the Division of Epidemiology at UT Southwestern, have solved the

mystery, showing through a detailed genetic study that the nerve gas sarin was largely responsible for the syndrome. The findings were published in *Environmental Health Perspectives*, a peer-reviewed journal supported by the National Institute of Environmental Health Sciences, with an accompanying editorial on the paper by leading environmental epidemiologists.

Dr. Haley's research group not only discovered that veterans with exposure to [sarin](#) were more likely to develop GWI, but also found that the risk was modulated by a gene that normally allows some people's bodies to better break down the nerve gas. Gulf War veterans with a weak variant of the gene who were exposed to sarin were more likely to develop symptoms of GWI than other exposed veterans who had the strong form of the gene.

"Quite simply, our findings prove that Gulf War illness was caused by sarin, which was released when we bombed Iraqi chemical weapons storage and production facilities," said Dr. Haley, a medical epidemiologist who has been investigating GWI for 28 years. "There are still more than 100,000 Gulf War veterans who are not getting help for this illness and our hope is that these findings will accelerate the search for better treatment."

In the years immediately following the Gulf War, more than a quarter of the U.S. and coalition veterans who served in the war began reporting a range of chronic symptoms, including fatigue, fever, night sweats, memory and concentration problems, difficulty finding words, diarrhea, sexual dysfunction, and chronic body pain. Since then, both [academic researchers](#) and those within the military and Department of Veterans Affairs have studied a list of possible causes of GWI, ranging from stress, vaccinations, and burning oil wells to exposure to pesticides, nerve gas, anti-nerve gas medication, and depleted uranium.

Over the years, these studies have identified statistical associations with several of these, but no cause has been widely accepted. Most recently, Dr. Haley and a colleague reported a large study in *Scientific Reports* testing veterans' urine for depleted uranium that would still be present if it had caused GWI and found none.

"As far back as 1995, when we first defined Gulf War illness, the evidence was pointing toward nerve agent exposure, but it has taken many years to build an irrefutable case," said Dr. Haley, who holds the U.S. Armed Forces Veterans Distinguished Chair for Medical Research, Honoring Robert Haley, M.D., and America's Gulf War Veterans.

Sarin is a toxic man-made nerve agent, first developed as a pesticide, that has been used in [chemical warfare](#); its production was banned in 1997. When people are exposed to either the liquid or gas form, sarin enters the body through the skin or breathing and attacks the nervous system. High-level sarin often results in death, but studies on survivors have revealed that lower-level sarin exposure can lead to long-term impairment of brain function. The U.S. military has confirmed that chemical agents, including sarin, were detected in Iraq during the Gulf War. In particular, satellite imagery documented a large debris cloud rising from an Iraqi chemical weapons storage site bombed by U.S. and coalition aircraft and transiting over U.S. ground troop positions where it set off thousands of nerve gas alarms and was confirmed to contain sarin.

Previous studies have found an association between Gulf War veterans who self-reported exposure to sarin and GWI symptoms. However, critics have raised questions of recall bias, including whether veterans with GWI are simply more likely to remember and report exposure due to their assumption that it may be linked to their illness. "What makes this new study a game-changer is that it links GWI with a very strong gene-environment interaction that cannot be explained away by errors in

recalling the environmental exposure or other biases in the data," Dr. Haley said.

In the new paper, Dr. Haley and his colleagues studied 508 deployed veterans with GWI and 508 deployed veterans who did not develop any GWI symptoms, all randomly selected from more than 8,000 representative Gulf War-era veterans who completed the U.S. Military Health Survey. They not only gaged sarin exposure—by asking whether the veterans had heard chemical nerve gas alarms sound during their deployment—but also collected blood and DNA samples from each [veteran](#).

The researchers tested the samples for variants of a gene called PON1. There are two versions of PON1: the Q variant generates a blood enzyme that efficiently breaks down sarin while the R variant helps the body break down other chemicals but is not efficient at destroying sarin. Everyone carries two copies of PON1, giving them either a QQ, RR or QR genotype.

For Gulf War veterans with the QQ genotype, hearing nerve agent alarms—a proxy for chemical exposure—raised their chance of developing GWI by 3.75 times. For those with the QR genotype, the alarms raised their chance of GWI by 4.43 times. And for those with two copies of the R gene, inefficient at breaking down sarin, the chance of GWI increased by 8.91 times. Those soldiers with both the RR genotype and low-level sarin exposure were over seven times more likely to get GWI due to the interaction per se, over and above the increase in risk from both risk factors acting alone. For genetic epidemiologists, this number leads to a high degree of confidence that sarin is a causative agent of GWI.

"Your risk is going up step by step depending on your genotype, because those genes are mediating how well your body inactivates sarin," said Dr.

Haley. "It doesn't mean you can't get Gulf War illness if you have the QQ genotype, because even the highest-level genetic protection can be overwhelmed by higher intensity exposure."

This kind of strong gene-environment interaction is considered a gold standard for showing that an illness like GWI was caused by a particular environmental toxic exposure, he added. The research doesn't rule out that other chemical exposures could be responsible for a small number of cases of Gulf War illness. However, Dr. Haley and his team carried out additional genetic analyses on the new data, testing other factors that could be related, and found no other contributing causes.

"There's no other risk factor coming anywhere close to having this level of causal evidence for Gulf War illness," said Dr. Haley.

The team is continuing research on how GWI impacts the body, particularly the immune system, whether any of its effects are reversible, and whether there are biomarkers to detect prior sarin exposure or GWI.

More information: Robert W. Haley et al, Evaluation of a Gene–Environment Interaction of PON1 and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey's National Population Sample, *Environmental Health Perspectives* (2022). [DOI: 10.1289/EHP9009](https://doi.org/10.1289/EHP9009)

Marc G. Weisskopf et al, Invited Perspective: Causal Implications of Gene by Environment Studies Applied to Gulf War Illness, *Environmental Health Perspectives* (2022). [DOI: 10.1289/EHP11057](https://doi.org/10.1289/EHP11057)

Randall R. Parrish et al, Resolving whether inhalation of depleted uranium contributed to Gulf War Illness using high-sensitivity mass spectrometry, *Scientific Reports* (2021). [DOI: 10.1038/s41598-021-00000-0](https://doi.org/10.1038/s41598-021-00000-0)

[10.1038/s41598-021-82535-3](https://doi.org/10.1038/s41598-021-82535-3)

Provided by UT Southwestern Medical Center

Citation: Genetic study confirms sarin nerve gas as cause of Gulf War illness (2022, May 12)
retrieved 8 May 2024 from

<https://medicalxpress.com/news/2022-05-genetic-sarin-nerve-gas-gulf.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.