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## Health Problems in Persian Gulf War Veterans Higher Due to Chemical Exposure

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### Description

A study by researchers at the University of California, San Diego School of Medicine shows there is increasing evidence that high rates of illness in Persian Gulf War Veterans can be explained, in part, by exposure to certain chemicals, including pesticides and nerve agents.

Newswise — A study by researchers at the University of California, San Diego School of Medicine shows there is increasing evidence that high rates of illness in Persian Gulf War Veterans can be explained, in part, by exposure to certain chemicals, including pesticides and nerve agents. Veterans from the 1990-91 conflict have a higher rate of chronic, multi-symptom health problems than either non-deployed personnel or those deployed elsewhere. Symptoms routinely reported by these veterans include fatigue, muscle or joint pain, memory problems, trouble sleeping, rash and breathing problems.

“This evidence suggests that exposure to this certain class of chemical may be linked to elevated risk of health problems,” said Beatrice Golomb, M.D., Ph.D., associate professor of medicine at the UC San Diego School of Medicine, whose study will be published in the early online edition of the Proceedings of the National Academy of Sciences (PNAS) the week of March 10.

“Health issues among Gulf War veterans have been a concern for nearly two decades. Now, enough studies have been conducted, and results shared, to be able to say with considerable confidence that there is a link between chemical exposure and chronic, multi-symptom health problems,” said Golomb. “Furthermore, the same chemicals affecting Gulf War veterans may be involved in similar cases of unexplained, multi-symptom health problems in the general population.”

The study synthesized evidence regarding a class of chemicals known as acetylcholinesterase inhibitors (AChEis) and organophosphates (OP), which includes nerve gas chemicals. Some military personnel were exposed to nerve gas (sarin) when demolishing Iraqi munitions. Also, the pesticides used aggressively in Gulf regions to control sand flies and other insects fall in the same category of chemicals. This includes the carbamate pyridostigmine bromide (PB) pills originally given to service members to protect against potential nerve-agent exposure. (Note: As a result of an earlier RAND corporation report by Golomb outlining the risks of using such pills, military policy has been changed.)

The study linked exposure to each of these chemicals with the chronic, multi-symptom health problems in 25 to 33 percent of returning Gulf War veterans.

“There is evidence that genetics have something to do with how a body handles exposure to these chemicals,” said Golomb. “Some people are genetically less able to withstand these toxins and evidence shows that these individuals have higher chance of suffering the effects of exposure.” Specifically, illness is linked to lower activity of enzymes that detoxify AChEs, due to genetic variants. The enzymes known to be involved are paraoxonase (PON) for OPs, including sarin, and butyrylcholinesterase (BChE) for PB.

Among those service members given PB pills as a preventive measure, those with the mutations that reduced their ability to detoxify the pills were at significantly higher risk of illness, according to Golomb.

Previous studies have shown genetic variants of these enzymes are also associated with increased rates of some neurological diseases, such as amyotrophic lateral sclerosis (ALS) or Lou Gehrig’s disease. Golomb says this may explain the elevated levels of ALS seen in Gulf War veterans.

Some of the chemicals linked to these multi-symptom illnesses continue to be used in agriculture, and at homes and offices for pest control in the United States and around the globe. Studies not related to the Gulf War showed that agricultural workers exposed to organophosphate pesticides had 10 times the number of health symptoms as those not exposed.

“Again, genetic variants that hamper defense against these chemicals were linked to higher risk of health problems. These findings carry important implications for current members of the armed forces as well as the general public, suggesting that exposure to these pesticides in any setting may increase risk for impaired neuropsychological function and poor health” said Golomb.

[http://afp.google.com/article/ALeqM5jNWhc19rHp-kdUNAX7b\\_tn87mZJQ](http://afp.google.com/article/ALeqM5jNWhc19rHp-kdUNAX7b_tn87mZJQ)

## **Gulf War syndrome firmly linked to chemical exposure**

**3 hours ago**

**CHICAGO (AFP)** — Nearly two decades after veterans of the 1991 Gulf War came home complaining of odd illnesses, enough evidence has been gathered to determine that many of them were sickened by chemical exposure, a study published Monday concluded.

And some of the damage was likely caused by pills prescribed to protect against the use of nerve gas and pesticides used to control sand flies, according to the study published in the Proceedings of the National Academy of Sciences.

While the military has subsequently stopped using the pills, the pesticides continue to be used in agriculture and for pest control in homes and offices in the United States and around the globe.

"Enough studies have been conducted, and results shared, to be able to say with considerable confidence that there is a link between chemical exposure and chronic, multi-symptom health problems," said study author Beatrice Golomb of the University of California San Diego's school of medicine.

"Furthermore, the same chemicals affecting Gulf War veterans may be involved in similar cases of unexplained, multi-symptom health problems in the general population."

Golomb examined the results of scores of studies looking at the health impact of the class of chemicals to which the veterans were exposed either through pesticides, the anti-nerve gas pills or the demolition of a weapons depot containing the nerve gas sarin.

Her study linked exposure to the chemicals to Gulf War syndrome, a chronic health problem which affected between 26 and 32 percent of deployed troops.

Symptoms routinely reported by these veterans include memory problems, trouble sleeping, muscle or joint pain, fatigue, rashes and breathing problems.

While the findings "do not imply that all illness in Gulf War veterans" is the result of this exposure it "may account for some or perhaps much of the excess illness seen in Gulf War veterans" she concluded.

Golomb also discovered why some veterans were sickened while others with equal or greater chemical exposure were not affected.

"There is evidence that genetics have something to do with how a body handles exposure to these chemicals," Golomb said.

"Some people are genetically less able to withstand these toxins and evidence shows that these individuals have higher chance of suffering the effects of exposure."

Some 250,000 service members were given the bromide pills as a preventative measure. Those with the mutations that reduced their ability to detoxify the pills were at significantly higher risk of illness, Golomb found.

Previous studies have shown that this mutation is also linked to increased rates of some neurological diseases, such as amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease.

# Gulf War Illness Strongly Linked to Chemical Exposure

Review found vets with the syndrome were more exposed to particular compounds

By **Amanda Gardner**  
*HealthDay Reporter*

MONDAY, March 10 (HealthDay News) -- A new scientific review finds a strong association between exposure to certain chemicals and the Gulf War illness suffered by many veterans.



The class of chemicals, known as acetylcholinesterase inhibitors (AChEIs), are found in pesticides, nerve agents and in pills given to soldiers to protect against nerve agents. The review, which was conducted by researchers at the University of California, San Diego, looked at 115 papers on the topic.

"Some of this has been stated for a while," said Joy Ray Miller, an assistant professor of pharmacy practice at the Irma Lerma Rangel College of Pharmacy at Texas A&M Health Science Center. "This article pulls it all together. It's definitely something to be aware of for our future veterans and for the military that's out there now. There are so many variants in the article that we can't really say as a matter of fact that [AChEIs cause the symptoms], but I think there are enough coincidences going on that we can have a pretty good understanding that maybe we should do something differently."

Veterans of the 1990-1991 Persian Gulf War have a higher rate of "chronic multi-symptom health problems" than either non-deployed military personnel or those deployed in other regions. In fact, 26 percent to 32 percent of personnel deployed to the Persian Gulf during this period have chronic health problems, a range that may actually understate the magnitude of the problem, according to the study, published in this week's issue of the *Proceedings of the National Academy of Sciences*.

Symptoms of the syndrome include fatigue, mood-cognition problems and musculoskeletal symptoms.

Although the exact causes remain unknown, evidence is mounting to suggest that exposure to organophosphate and carbamate acetylcholinesterase inhibitors (AChEIs), including pyridostigmine bromide (PB), pesticides and nerve agents, may be responsible.

The authors of this paper looked at epidemiological studies assessing the link between these chemicals and symptoms observed in Gulf War vets.

Many of the studies reported a link between exposure to AChEI and chronic symptoms.

An estimated 250,000 personnel received the carbamate pyridostigmine bromide (PB) as a pretreatment for potential exposure to nerve agents. Those who took more pills had a higher incidence of symptoms.

Also, an estimated 41,000 service members may have been overexposed to pesticides, which were used to control vector-borne disease, and 100,000 personnel may have been exposed to low levels of sarin nerve agent after the demolition of the Khamisiyah munitions depot in Iraq.

The symptoms are akin to those suffered by agricultural workers exposed to AChEIs, said the study authors, as well as symptoms suffered by victims of the sarin terrorist attacks in Japan.

Exposure to AChEIs could also be linked to the higher rate of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, in Gulf War veterans. Sporadic ALS has been associated with exposure to agricultural chemicals.

And men and women with the Gulf War symptoms were more likely to have lower concentrations and activity levels of enzymes which work to clear AChEIs from the system. Genetics may impact the way the body processes these chemicals, specifically the actions of these related enzymes.

"They're giving certain people so many of these nerve agent pills or pesticides, and [the authors] say that some people metabolize them and some not," Miller said. "Are we really giving a toxic dose apart from the genetics? What are they giving and have they really tested the amounts that they're giving? Are we overdosing?"

### **More information**

There's more on Gulf War syndrome at the [University of Chicago Medical Center](#).

SOURCES: Joy Ray Miller, Pharm.D., assistant professor, pharmacy practice, Irma Lerma Rangel College of Pharmacy, Texas A&M Health Science Center, Kingsville; March 10-14, 2008, *Proceedings of the National Academy of Sciences*

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# Gulf War syndrome's chemical-origin theory upheld

**A class of compounds found in nerve gas and pesticides remains the likely cause, a review of studies concludes.**

By Jia-Rui Chong, Los Angeles Times Staff Writer  
March 11, 2008

A review of medical studies on Gulf War syndrome supports the theory that the still-hazy disorder was caused by a group of related chemicals found in pesticides used around military facilities and anti-nerve-gas pills given to soldiers, according to a study released Monday.

A similar chemical was also found in nerve gas that was inadvertently released when U.S. soldiers destroyed a munitions depot just after the 1991 war, according to the study published in the Proceedings of the National Academy of Sciences.

The group of chemicals, known as acetylcholinesterase inhibitors, has long been discussed as a possible cause of Gulf War syndrome.

The review "thoroughly, conclusively shows that this class of chemicals actually are a cause of illness in Gulf War veterans," said Dr. Beatrice Golomb, an associate professor of medicine at UC San Diego and the author of the latest paper.

Other researchers, however, said the syndrome's symptoms are so varied that it's probably difficult to place the blame on a single cause.

"It seems clear at this point, 17 years beyond the conflict, that the chances we will ever resolve this with any single 'smoking gun' exposure grows smaller with time," said Dr. Charles Engel, director of the Department of Defense Deployment Health Clinical Center at Walter Reed Army Medical Center in Washington.

Gulf War syndrome is a complex -- and controversial -- illness typically characterized by a variety of symptoms, including fatigue, muscle or joint pain and mood problems. About 200,000 veterans are believed to suffer from it, according to the study.

But there is still uncertainty. A panel of the federal Institute of Medicine said in 2006 that it could not say if there was a coherent set of symptoms that pointed to an identifiable syndrome.

Researchers have proposed a number of potential causes, including psychological stress and exposure to toxic materials from oil-well fires and depleted-uranium ammunition, experts said.

In toxic doses, acetylcholinesterase inhibitors cause unbridled signaling between cells, potentially

leading to muscle paralysis, seizures and excess secretion in the airways.

Previous studies have estimated that at least 250,000 soldiers were exposed to some form of the chemical.

Golomb's study looked at more than 70 studies on Gulf War syndrome and acetylcholinesterase inhibitors.

She found that 18 of the 21 epidemiological studies looking at chronic health problems in Gulf War veterans showed a connection to at least one kind of acetylcholinesterase inhibitor exposure.

Golomb also noted several studies that found sick veterans were more likely to have an enzyme problem that lowered their ability to clear the chemicals from their bodies.

Several studies also found Gulf War syndrome-like symptoms in farmworkers exposed to pesticides and victims of the 1995 sarin gas attacks in Japan. Some of the studies showed similar enzyme deficiencies.

The analysis found few studies that confirmed connections to other causes for Gulf War syndrome.

"The importance of this paper is that it brings together research from different realms, which are all parallel and point in the same direction," said Lea Steele, an epidemiologist who has served as scientific advisor to the Department of Veterans Affairs. She was not involved in the analysis.

Engel, of Walter Reed, said he was unconvinced -- in part because there is little, if any, accurate measurement of chemical exposures during the war.

"It is well known that significant error results from looking back years after the fact and asking people to try to recall potential exposures," he said.

# Acetylcholinesterase inhibitors and **Gulf War** illnesses

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## Abstract

Increasing evidence suggests excess illness in Persian **Gulf War** veterans (GWV) can be explained in part by exposure of GWV to organophosphate and carbamate acetylcholinesterase inhibitors (AChEis), including pyridostigmine bromide (PB), pesticides, and nerve agents. Evidence germane to the relation of AChEis to illness in GWV was assessed. Many epidemiological studies reported a link between AChEi exposure and chronic symptoms in GWV. The link is buttressed by a dose–response relation of PB pill number to chronic symptoms in GWV and by a relation between avidity of AChEi clearance and illness, based on genotypes, concentrations, and activity levels of enzymes that detoxify AChEis. Triangulating evidence derives from studies linking occupational exposure to AChEis to chronic health symptoms that mirror those of ill GWV. Illness is again linked to lower activity of AChEi detoxifying enzymes and genotypes conferring less-avid AChEi detoxification. AChEi exposure satisfies Hill's presumptive criteria for causality, suggesting this exposure may be causally linked to excess health problems in GWV.