LETTER

Acetylcholinesterase inhibition and Gulf War illnesses: Conclusions are not supported by independent reviews of the same evidence

To the Editor: Golomb (1) concludes that there is strong evidence that exposure to acetylcholinesterase inhibitors [e.g., nerve agents, pyridostigmine bromide (PB), and pesticides] caused illness in 1991 Gulf War veterans (GWVs). We neither agree with her interpretation of the literature, including our own work, nor her conclusions, and believe she has neglected research that does not support her views.

The reported increase in extra cases of ALS in U.S. GWVs reported in one paper is an important part of her argument, and she makes inferences about possible links between ALS and acetylcholinesterase inhibitors. However, the excess was small, there was a strong possibility that cases were overascertained among GWVs, and the control sample had an unusually low incidence of ALS (2, 3). There is no increase in deaths from neurological causes in GWVs. The increase in ALS is in veterans of wars not associated with anticholinesterases, which is evidence against, not in favor, of her hypothesis.

Golomb does not mention the numerous large, representative, controlled, investigations of Gulf veterans, all of which concluded that there was no evidence of damage to the peripheral nervous system that could be accounted for by exposure to organophosphate-containing compounds (e.g., ref. 4).

Golomb quotes extensively many of our papers that have identified associations between neurological symptoms and self-reported exposure to pesticides, PB, and nerve gas but, unlike the original authors, does not pay any attention to recall bias. Finally, Golomb ignores a series of authoritative and extensive reports, such as those produced by the prestigious and independent Institute of Medicine (5, 6) and others, which have undertaken scholarly reviews of the same literature and come to very different conclusions.

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- 1. Golomb BA (2008) Acetylcholinesterase inhibitors and Gulf War illnesses. *Proc Natl Acad Sci USA* 105:4295–4300.
- Rose M (2003) Gulf war service an uncertain trigger for ALS. *Neurology* 61:730–731.
- Armon C (2007) Occurrence of amyotrophic lateral sclerosis among Gulf War Veterans. *Neurology* 68:1083.
- Sharief M, et al. (2002) Neurophysiologic evaluation of neuromuscular symptoms in UK Gulf War veterans: A controlled study. *Neurology* 59:1518–1525.
- 5. Institute of Medicine (2000) Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines (Natl Acad Sci, Washington), Vol 1.
- 6. Committee on Gulf War and Health (2004) *Gulf War and Health: Updated Literature Review of Sarin* (Natl Acad Sci, Washington).

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