

**Presentation 5 – Nelda Wray**



Relationship between  
Illnesses in Gulf War Veterans and  
Acetylcholinesterase Levels

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Principal Investigators

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- Hermona Soreq, Ph.D., Hebrew University, Jerusalem

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VA Collaboration with Dr. Soreq

- In Feb. 2003, Dr. Wray attended meeting of Research Advisory Committee on Gulf War Veterans' Illnesses.
- Very exciting presentation by Dr. Soreq, a leading researcher in field of neurotransmitters (chemicals that transmit signals in nervous system).
- Dr. Wray decided that VA should collaborate with Dr. Soreq to study illnesses in Gulf War veterans.
- This study was placed on fast track for planning and funding.

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Background on  
Acetylcholinesterase and Illness

- Acetylcholinesterase (AChE) is an essential enzyme involved in transmission of signals between nerve cells.
- Abnormalities of AChE metabolism occur in neurological diseases:
  - Alzheimer's disease
  - Myasthenia gravis
- Some medications cause changes in AChE levels:
  - Some anti-depressants inhibit AChE activity (lower levels).
  - Some anti-psychotics induce release of AChE (higher levels).

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### Recent Study of Human AChE Levels by Dr. Soreq

- 470 members of American population.
- Strong correlation between levels of illness and serum AChE levels.
- As the reported levels of illness increased, the AChE levels decreased.
- No correlation between illness levels and levels of two other enzymes related to acetylcholine metabolism:
  - BuChE (Butyrylcholinesterase)
  - PON (Paraoxonase)

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### Exposure to AChE Inhibitors During the Gulf War

- During Gulf War, troops were potentially exposed to a number of chemicals that inhibit AChE:
  - Pyridostigmine bromide (PB)
  - Organophosphate pesticides (e.g., chlorpyrifos)
  - Low levels of nerve agents (e.g., sarin)
- Dr. Soreq's hypothesis:
  - Exposure to these chemicals could lead to long-term alteration of AChE function, which could lead to illnesses in some Gulf War veterans.

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### Objective of Collaborative VA-Israeli Study

- To determine if serum levels of AChE are related to illnesses in Gulf War veterans and non-deployed veterans.

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### Collaborative Roles of Research Team

- Dr. Doebbeling and Iowa scientists:
  - Provide frozen serum samples
  - Provide data on illnesses in Gulf War and non-deployed veterans
- Dr. Soreq and Israeli scientists:
  - Analyze serum samples for levels of AChE
- Statistical analysis by Cooperative Studies Program in West Haven, CT

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### Participants in Iowa Study

- Phase I:
  - In 1995-96, 3,695 veterans took part in telephone interviews.
  - 50% Gulf War veterans, 50% non-deployed veterans
- Phase II:
  - In 1999-2002, a subset of 580 veterans took part in detailed medical exams, including serum samples.
  - 50% Gulf War (GW) veterans; 50% non-deployed (ND) veterans
  - Four groups were evaluated (3 ill groups and one control group):
    - Ill: Cognitive dysfunction, Depression, or Chronic Widespread Pain (both GW and ND veterans)
    - Healthy controls: both GW and ND veterans
  - Frozen sera are available for these 580 veterans.

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### Planned Statistical Analysis

- Compare levels of AChE among Gulf War veterans vs. non-deployed veterans.
- Compare levels of AChE among ill veterans vs. healthy veterans.

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### Timeline of Study Development and Implementation

- Feb. 2003: Dr. Wray meets Dr. Soreq and decides that VA should perform collaborative research with her.
- April 2003: Cooperative Studies Program planning meeting held with Dr. Soreq and Dr. Doebbeling.
- May 2003: Proposal written and IRB approval.
- June 2003: Shipment of serum samples to Israel.
- Late summer 2003: Preliminary results expected.

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### Significance of Collaborative Research

- In 1999, RAND Corporation report on potential health effects of pyridostigmine bromide in Gulf War veterans.
  - Recommended that a study similar to this VA study with Dr. Soreq would be one of the definitive studies of illnesses in Gulf War veterans.
- This study could lead to better understanding of the underlying biochemical mechanism of illnesses in some Gulf War veterans.
- This collaborative research is responsive to recommendations of *Interim Report* of Research Advisory Committee on Gulf War Veterans' Illnesses.

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