


Presentation 5 – Nelda Wray



Relationship between
Illnesses in Gulf War Veterans and
Acetylcholinesterase Levels


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Principal Investigators

- Bradley Doebbeling, M.D., Iowa City VA Medical Center and University of Iowa
- 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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