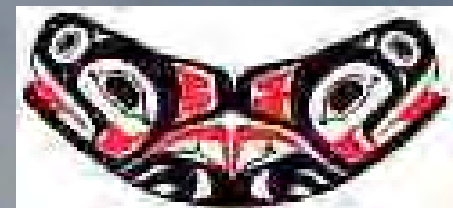


US EPA ARCHIVE DOCUMENT

Washington State Cholinesterase Monitoring Program: An Applied Biomarker in Public Health

Matthew Keifer MD MPH
Endowed Chair, Agricultural Medicine
National Farm Medicine Center
Marshfield WI and Adjunct Professor of
Public Health
University of Washington



What I will Discuss

- Cholinesterase as a biomarker/diagnostic test
- Cholinesterase monitoring in Washington State
- A study of risk factors for cholinesterase depression
- What is the impact of WA ChE monitoring program
- How the information is being used

Acknowledgements

PNASH

- Jon Hofmann
- Harvey Checkoway
- Gerald van Belle
- Clem Furlong
- Lesley Hoare
- Maria Negrete
- Pablo Palmandez

Central Washington

Occupational Medicine

Pam Ernst and Joe Cozzetto

Betty Anne Cohen

Washington State Department of Agriculture

Ofelio Borges

Flor Servin

Furlong lab

- Toby Cole
- Jerry Kim
- Rebecca Richter
- Rick Stevens
- Stephanie Suzuki

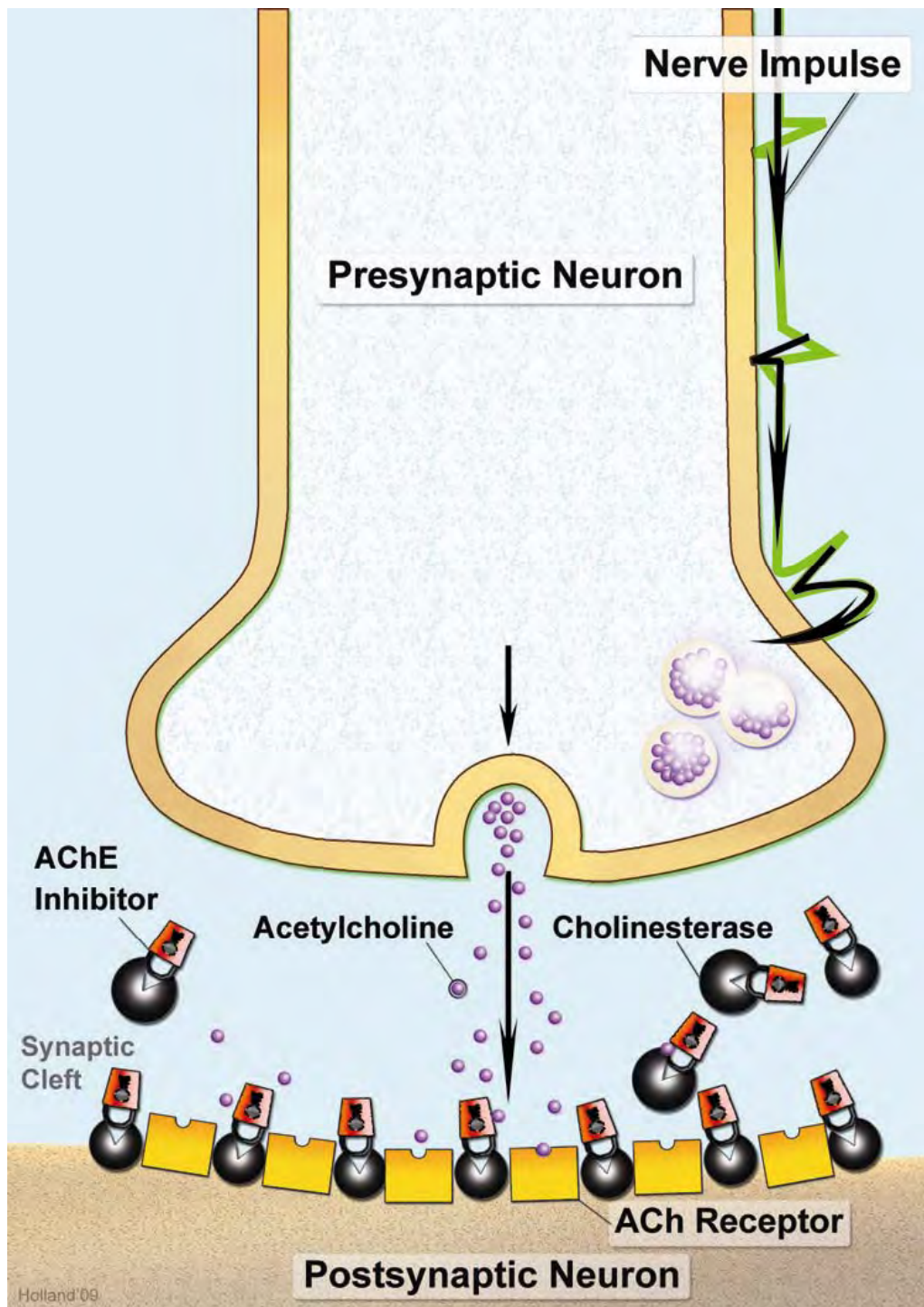
CEEH Functional Genomics lab

- Fred Farin
- Zahra Afsharinejad

Washington Dep L&I

- John Furman RN PhD.

•Financial support for this project was provided by CDC/NIOSH grants #U50-OH07544 and #T42-OH008433-01, and NIEHS grants #P30-ES07033, #T32-ES07262, and #P42-ES04696



Acetylcholine a chemical transmitter in CNS & PNS

Acetylcholinesterase (AChE)

- Hydrolyzes acetylcholine

2 ChE's present in blood

- AChE associated with RBC membranes
- Butyrylcholinesterase (BuChE) in serum

Cholinesterase: the Test

The Only Commonly Available Test for Pesticides

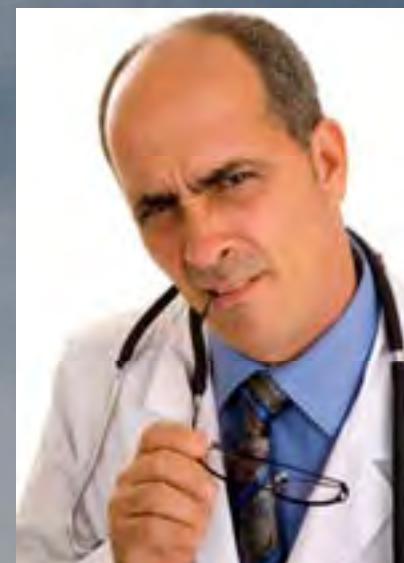
- Advantages
 - Covers 2 important chemical groups
 - Well established methods
 - Widely done clinically
 - Well known to clinicians
 - Measures toxicologic target of the pesticide



Cholinesterase: the Test

The Only Commonly Available Test for Pesticides

- Disadvantages
 - Poorly understood- "the only pesticide test"
 - Wide normal range- Mayo Clinic NL Range : 3100-6500
 - Requires baseline for accuracy
 - Acetylcholinesterase is a challenging test
 - Affected by some medications and illnesses
 - Recovery in weeks to months



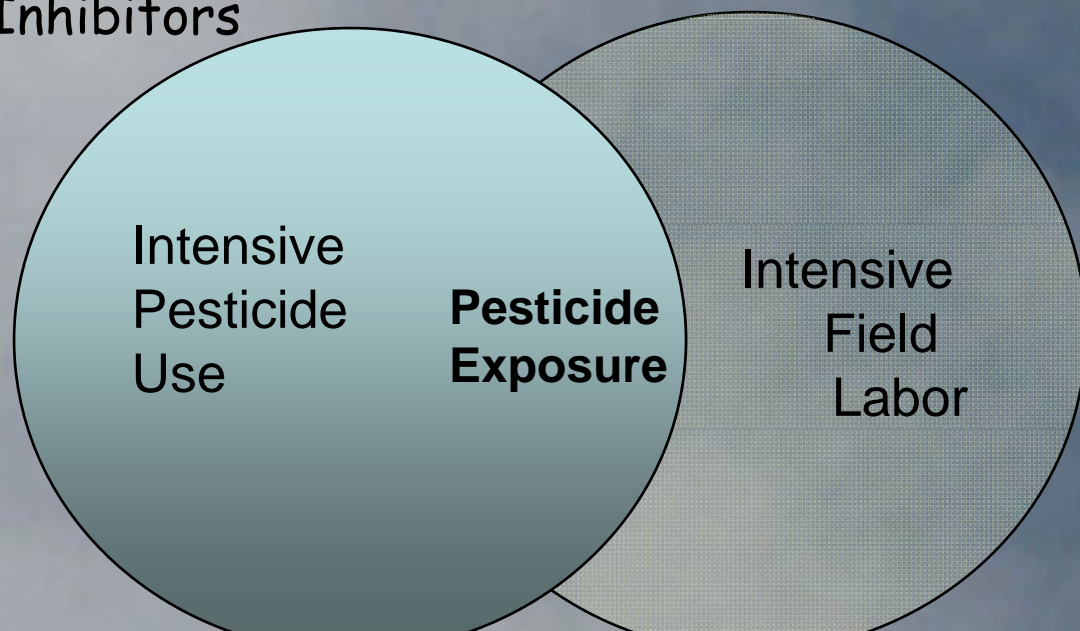
Cholinesterase Monitoring

Biomarker for OP and carbamate exposure

- California has oldest state ChE requirement in US, required since 1974
 - Filmore and Lessenger (1993) - Found 24% of workers had ChE depression requiring removal in California program
 - Ames et al. (1985) found that 5% of 500+ samples on CA workers required removal
 - 31% were ill.
 - -cooperation on data call in was poor.

Washington Workers and Pesticides

- Crops
 - Apples, Pears, Cherries, Hops, Potatoes, Chickens
- Workers
 - 100,000+ Agricultural Workers at peak
- Pesticide Incident Reporting Panel
 - 250-400 Pesticide Poisonings per year
 - 50% Agricultural
 - 1/3 Cholinesterase Inhibitors



Rios V. Dept Labor and Industries 2002- WA Supreme Court



"L&I Do Your Duty" Monitor for
ChE Depression

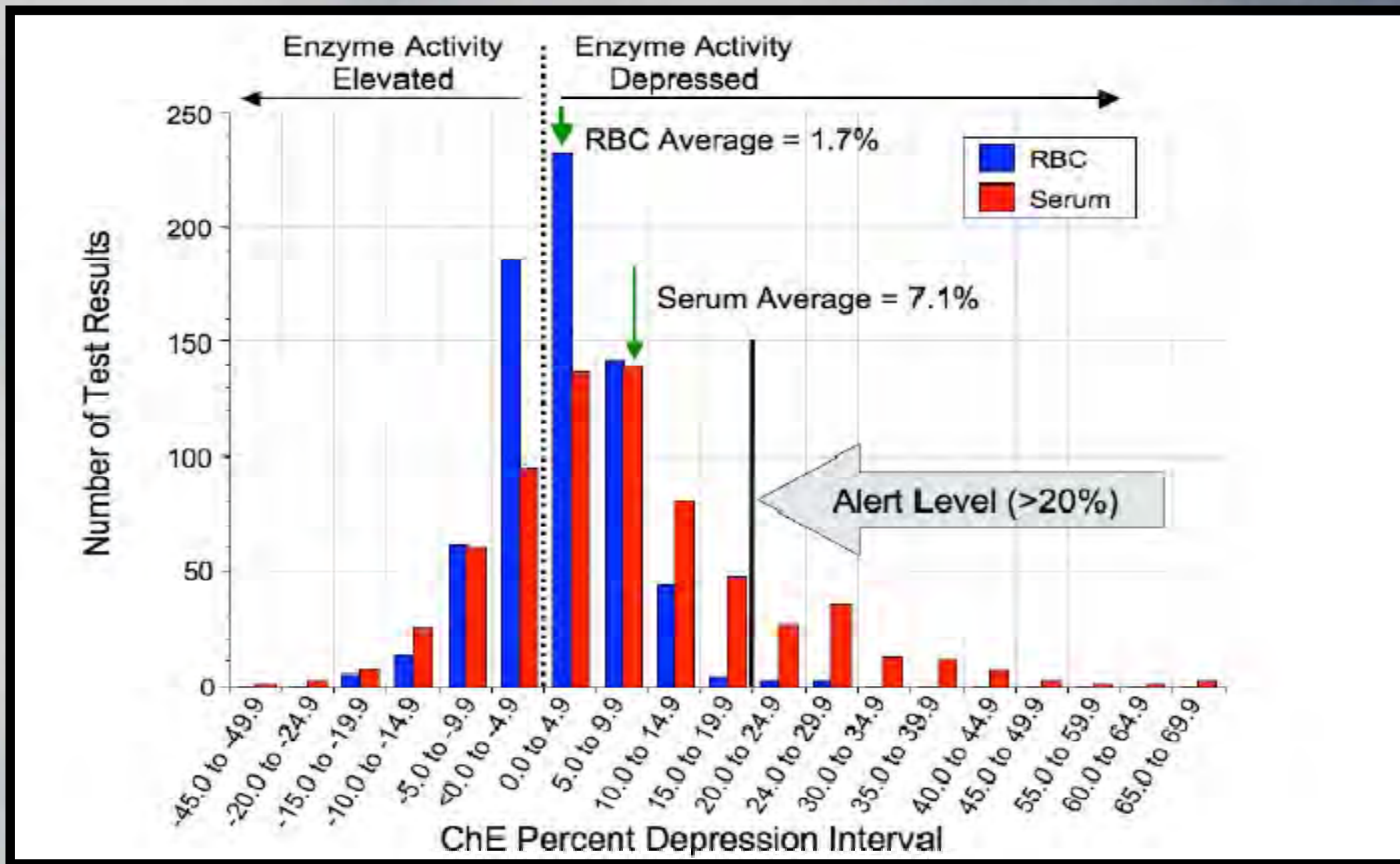
Cost Benefit Determination and Small Business Impact Statement of Cholinesterase Monitoring (Dep L&I)

- Prevention of illness after over-exposure.
- Increase hazard awareness and improve overall workplace safety related to pesticide use.
- Improve pesticide illness diagnosis and reporting.
- Provide greater certainty about frequency of pesticide over-exposure.
- Decrease the risk of unintended exposures to workers families.

How the System Works

- Before exposure
 - January-March workers who will spray and reach threshold undergo baseline testing
- During season
 - March -August workers who reach threshold undergo follow-up testing
- Depressions
 - 20% review work practices
 - 30% Ache or 40% PChE - removal from exposure

Cholinesterase Results 2006 Report: Change from Baseline



Mean change in BChE and AChE significant at $p < 0.00$

A Study of the Risk Factors for ChE Depression

1. Recruit workers at Che follow-up testing
2. Collect workplace information and evaluate how these factors influence BuChE inhibition
3. Evaluate the relationship between PON1 status and serum cholinesterase (BuChE) inhibition



Presione 'seguir' para pasar a la siguiente pantalla

En los últimos 30 días, ¿en cuál de los siguientes cultivos aplicó pesticidas?
Seleccione todas las respuestas que apliquen, luego presione "seguir" para pasar a la siguiente pantalla.



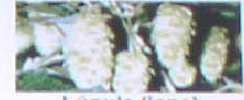
Manzanas



Cerezas



Uvas



Lúpulo (jape)



Peras



Duraznos



Chabacanos



Ciruelas



Algún otro u otros cultivos



No aplico pesticidas



No sé

Terminar



Apagar el sonido



Volver

No quiero contestar

OP/CB exposure score

- Based on algorithm from the Agricultural Health Study (Dosemeci *et al.*, 2002; Coble *et al.*, 2005; Hines *et al.*, 2008)

Work activity score

- Toxicity * $\overbrace{(\text{Handle} + \text{Apply} + \text{Clean})}^{\text{Work activity score}} * \text{PPE}$
- Characterizes exposure intensity for past 30 days

Results

Mixing/loading Pesticides

- Potential for higher levels of exposure
- Splashes, spills, contact with contaminated equipment
- Exposure to concentrated product



USDA, 2006

Cleaning Spray Equipment

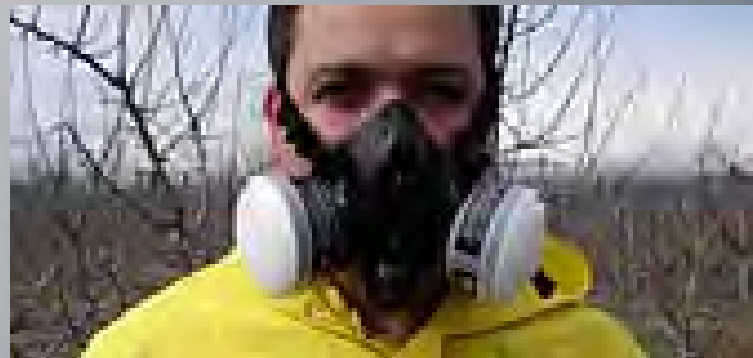
- Associated with elevated urinary levels of 2,4-D in study by Arbuckle *et al.* (2002)
- Handlers may not wear PPE for cleaning activities



USDA, 2006

Half-face Respirators

- Half-face respirator use reported in many investigations of ChE depression by L&I



- Potential for dermal contamination on upper portion of face

Footwear and Lockers

- Take home exposure pathway
 - Wearing work boots home
 - Not using a locker



- May be surrogates for other sources of exposure

Glove Use

- Other studies have shown that glove use is one of the most effective ways of reducing exposure (de Cock 1995, Arbuckle 2002)
- Why don't we see an association in our study?
 - Chemical-resistant glove use nearly universal
 - Consequently, we can only assess use of other gloves in combination with chemical-resistant gloves



Depressions Have Decreased over 6 years

Year	Baselines		>20%
2010	1989	316	3.1%
2009	2056	286	8.8%
2008	2013	495	7.0%
2007	1857	386	12.6%
2006	1889	471	10.6%
2005	2263	611	8.0%
2004	2630	580	16.7%

Investigations by L&I

Depressions and Quitters

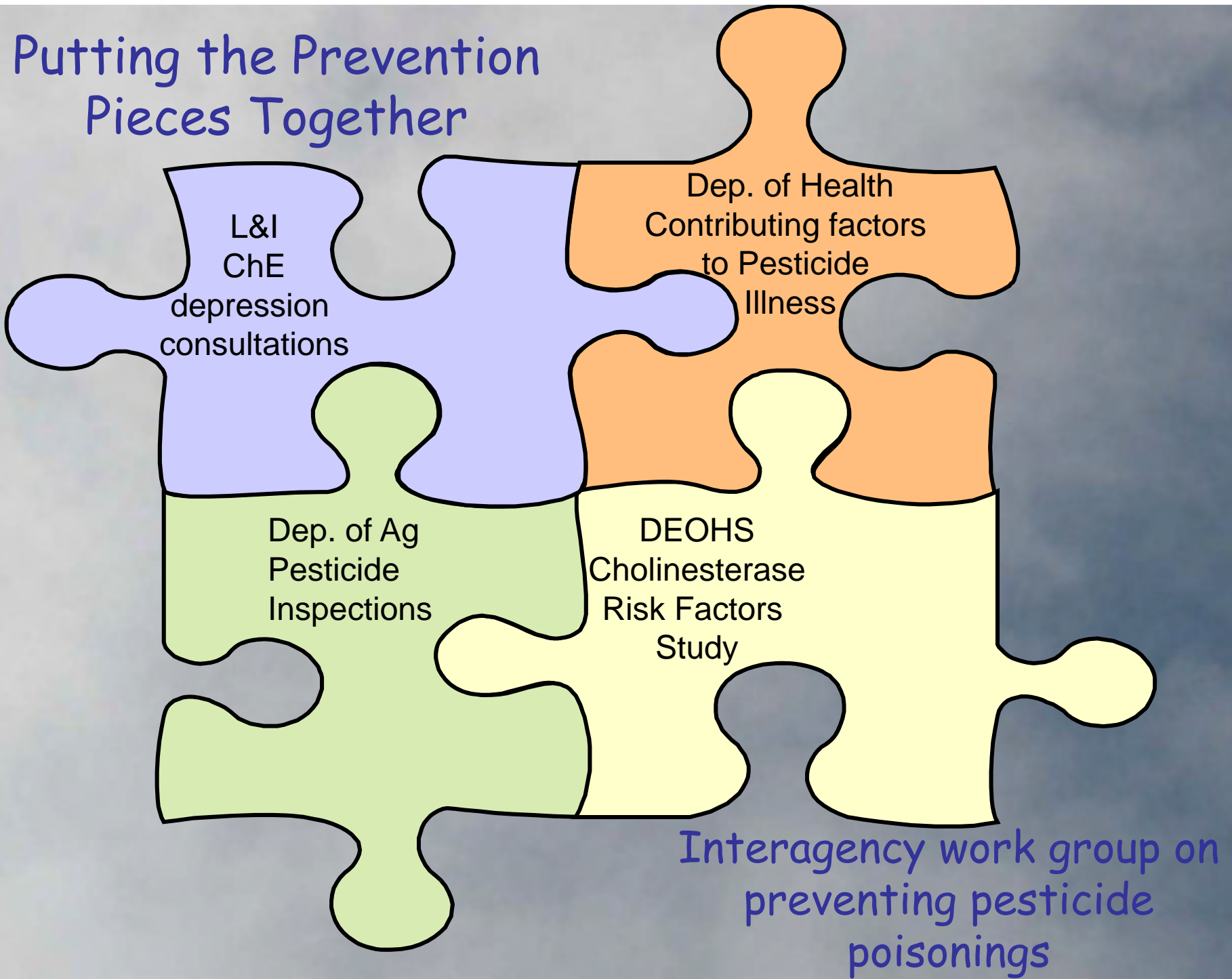
Depression Risk Factors?

- Airblast sprayer commonly reported in those with >20% depression
- Baseball cap use common as well
- Poor PPE management
- Poor workplace hygiene practices

Employers who stopped participating (30 interviewed)

- Owner applied pesticides
- Eliminated ChE inhibitors from arsenal
 - Changed pesticides to lower toxicity or other classes
 - Went organic
 - Increased IPM to decrease use
- Increased employees who applied
- Increased spray rate-decreased hours

Putting the Prevention Pieces Together



Conclusion

- ChE is an old and non-specific biomarker/diagnostic tool
- This tool can help identify where worker protection fails
- Interventions can be developed to reduce worker exposure
- The monitoring motivates change to different products and practices
- Newer biomarkers hold greater promise



Questions?