



# Pesticide Diagnostic Testing

*Give Me a Test  
I'll Give You a Diagnosis*

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# Objectives

- Understand the important role of clinicians in protecting workers through participation in the surveillance systems on pesticide health effects.
- Describe the logic behind the need for clinical tools for diagnosing pesticide poisonings.
- Describe the pivotal role that EPA plays in shaping the clinicians ability to accurately diagnose pesticide poisonings.



# Farmworker Protection 101

- What federal agency is responsible for worker health and safety, worker protection?
- *OSHA (Department of Labor)*
- What federal agency is responsible for farmworker protection?
- *EPA – Worker Protection Standard*



# Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

- Established registration for all pesticides
- Empowers EPA to require a great deal from pesticide registrants to protect the public from the health effects of these chemicals
- FIFRA stronger than law regulating other chemicals- Toxic Substance Control Act (TSCA)
- Because of FIFRA
  - We know a lot about pesticides... but we can know a lot more
  - Companies know a lot about their chemicals



# **FIFRA Mandates that EPA Protect Farmworkers**

## **Worker Protection Standard in 1972**

**Farmworkers DENIED overall protection from OSHA 1975**

United States Court of Appeals, District of Columbia Circuit.

“We agree and hold that EPA has the authority to promulgate rules regulating farmworker exposure to pesticides and by so doing has preempted the Secretary of Labor from acting.”

“Nothing in this (Act) shall apply to working conditions of employees with respect to which other Federal agencies . . . exercise statutory authority to prescribe or enforce standards or regulations affecting occupational safety or health.” OSH Act of 1970

Case: Organized Migrants in Community Action, Inc. v. Brennan, 520 F.2d 1161 (D.C. Cir. 1975).



## What OSHA Does

- 34 standards include worker monitoring components (includes 13 Carcinogens)
- Most standards covering chemicals have exposure assessment in some form
- OSHA general approach
  - Trust but verify- measure exposure, measure levels in the body, engineer controls, train/inform workers, set, measure and enforce exposure limits

# EPA's General Approach

- Count incidents from passive surveillance systems and act on that information
- Not one national standard for monitoring workers
- WPS
  - Provide PPE to workers
  - Train/inform workers
  - Establish entry intervals



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## What Do Matt and Amy Do?

- Pesticide Program Dialogue Committee
- Federal Advisory Committee to the US EPA Office of Pesticide Programs
- Offer a voice on a national level for farmworker protection
  - Farmworker Representative (Amy)
  - Public Health Representative (Matt)



# Outbreak of Phosdrin Poisonings Washington 1993



Images © PNASH

Phosdrin substituted for Phosphamidon for apple aphids



June 14, 1993

AMVAC requested WSDA safety rules

- observer present during mixing/loading
- Extend re-entry interval 48 -> 96 hrs
- Safety training for handlers
- Warning signs posted on all treated orchards



# Phosphamidon vs Phosdrin

Organophosphate Pesticides

## Phosphamidon

Oral (mouth) LD<sub>50</sub> 17 mg/kg

Dermal (skin) LD<sub>50</sub> 374 mg/kg



## Phosdrin

Oral (mouth) LD<sub>50</sub> 6.1 mg/kg

Dermal (skin) LD<sub>50</sub> 4.7 mg/kg

**Despite rules...  
27 workers became ill**

**DOH Pesticide Illness  
Surveillance detects  
4 case outbreak** →

**DOH reports outbreak  
to WSDA** →

Date of Incident	Work Activity	Age/Gender/Race	Vomiting	Nausea	Dizziness	Weakness	Visual Disturbance	Miosis	Headache	Abdominal pain	Diarrhea	"Funny Taste"	Shortness of Breath	Hypersecretion	Treatment Type	%RBC AChE Depr.	%Plasma ChE Depr.	L&I Claim Paid?	DOH Finding
6/13	Mixer	30MW	x	x		x	x			x				x	Admit	-	25%	yes	def
6/13	Sprayer	30MH	x	x						x					ER	-	-	yes	def
6/18	Sprayer	30MH	x	x	x		x								ER	41%	-	yes	def
6/18	Sprayer	29MH				x		x						x	Admit	6%	-	yes	def
7/7	Mixer	53MH	x	x										x	ER	75%	97%	yes	def
7/7	Thinner	39FH	x						x						ER	-	-	yes	unk
7/8	Well Dr	24MW	x	x							x	x			ER	WNL	WNL	yes	pro
7/8	Well Dr	34MW		x					x						ER	WNL	WNL	N/A	pos
7/8	Sprayer	39MH	x	x	x	x			x						ER	-	-	yes	def
7/10	Sprayer	44MH	x	x					x				x		Admit	71%	58%	yes	def
7/12	Mix/spr	19MH	x				x			x					ER	43%	64%	yes	def
7/13	Mixer	31MH			x				x					x	ER	-	-	yes	def
7/19	Mixer	28MH	x	x	x			x	x						ICU	-	56%	yes	def
7/19	Mixer	20MH	x	x	x		x								ER	57%	-	yes	def
7/20	Sprayer	27MH		x				x				x			ER	-	-	yes	def
7/21	Mixer	47MH	x	x			x	x		x				x	ICU	54%	76%	yes	def
7/22	Sprayer	41MH	x	x		x	x			x					ER	28%	-	yes	def
7/22	Sprayer	68MW	x	x			x	x			x		x		ICU	51%	WNL	yes	def
7/27	Sprayer	24MH	x	x	x	x			x						ER	8%	WNL	yes	def
7/29	Sprayer	72MW	x			x									ER	59%	42%	yes	pro
7/29	Sprayer	23MH	x	x	x	x	x			x					ER	50%	59%	yes	def
8/3	Observer	38MW						x							ER	-	-	yes	pro
8/7	Sprayer	31MH	x	x		x									ER	90%	-	yes	def
8/7	Mixer	23MW													ER	-	-	yes	def
8/12	Reentry	32MH	x	x	x		x		x	x					ER	WNL	WNL	yes	pro
8/12	Mixer	25MH		x					x						ER	62%	76%	yes	def
8/18	Mixer	57MW		x				x						x	ICU	-	47%	yes	def



# Public Health Response

## Blast Fax to ER's in Eastern WA - Phosdrin Alert

- signs and symptoms
- medical treatment
- protection for health care providers
- request to report all suspected cases to DOH

Reviewed all reported cases to find earlier cases

Provided summary of cases and medical outcomes to regulatory agencies





STATE OF WASHINGTON  
DEPARTMENT OF HEALTH  
OFFICE OF TOXIC SUBSTANCES

*Airustrial Center, Building 4 • P.O. Box 47825 • Olympia, Washington 98504-7825*

## **Attention Emergency Rooms: PHOSDRIN ALERT**

Twelve cases of phosdrin poisoning have been reported to the Washington State Department of Health since June 1993. Four, of the twelve cases, have resulted in hospital admission. Poisonings are occurring despite use of personal protective gear. Phosdrin is highly acutely toxic. Rapid recognition and treatment of poisoning is critical.

### **Phosdrin Toxicity**

Phosdrin (mevinphos) is an organophosphate insecticide. It has recently replaced a less toxic insecticide for aphid control on apples and pears in Eastern Washington.

Phosdrin is a potent cholinesterase inhibitor. It is easily absorbed through skin and highly acutely toxic via dermal and oral routes (rat LD50 oral = 4 - 7 mg/kg, rat LD50 dermal = 4 - 5 mg/kg). Its high volatility also constitutes an inhalation hazard.

Onset of symptoms is usually within 2 hours of acute exposure and may be within minutes after an inhalation exposure. Low level dermal exposures to contaminated clothing may result in delayed onset of symptoms.

Symptoms associated with phosdrin intoxication include: nausea, vomiting, dizziness, hypersecretion, miosis, blurred vision, diarrhea, muscle twitching, weakness, and impairment of judgement.

### **Medical Treatment**

Wear rubber gloves when decontaminating the patient or handling Phosdrin contaminated clothing. Save clothing in a clean plastic bag.

Collect blood for laboratory analysis of RBC and plasma cholinesterase activity.

Atropine is the antidote. Do not wait for confirmation of cholinesterase inhibition if patient has history of phosdrin exposure and has signs and symptoms of poisoning. Call Washington Poison Network for treatment advice (800) 732-6985.

## **Report Cases Immediately to Department of Health Pesticide Section (206) 753-5965**

Washington State Department of Health is investigating these cases to determine how exposures are occurring and is working with regulatory agencies to prevent future incidents. Your report is critical to this process.



August 24<sup>th</sup> 1993 - Seattle Post-Intelligencer

## Apple Pesticide a Threat.

Hospitalization of 11 farm workers heightens concern

August 31, 1993 – Seattle Post-Intelligencer

## Apple Pesticide Ban Ordered State cites hazard to farm workers

Three state agencies yesterday ordered Washington's Apple growers to halt immediately their use of Phosdrin...

**Really a “suspension”**





# Investigation into cause...

WSDA, L&I, DOH follow-up interviews:

- PPE available to all handlers, not always worn.
- Lack of experience with chemical so acutely toxic (esp. by skin route)
- Lack of required supervision/hazard training.
- Label not protective enough – some very ill despite following all label and state emergency rules.
  - Air blast sprayers a factor





# Regulatory Outcome

Spring 1994 - WA bans in tree fruit but allows continued use in peas, seed and vegetable crops.

June 9<sup>th</sup> – EPA announces it will take aggressive regulatory action

- High illness rate relative to use
- High severity of medical outcome

June 30<sup>th</sup> – Registrant voluntary cancels pesticide. Pesticide removed from the market. Existing stocks allowed.



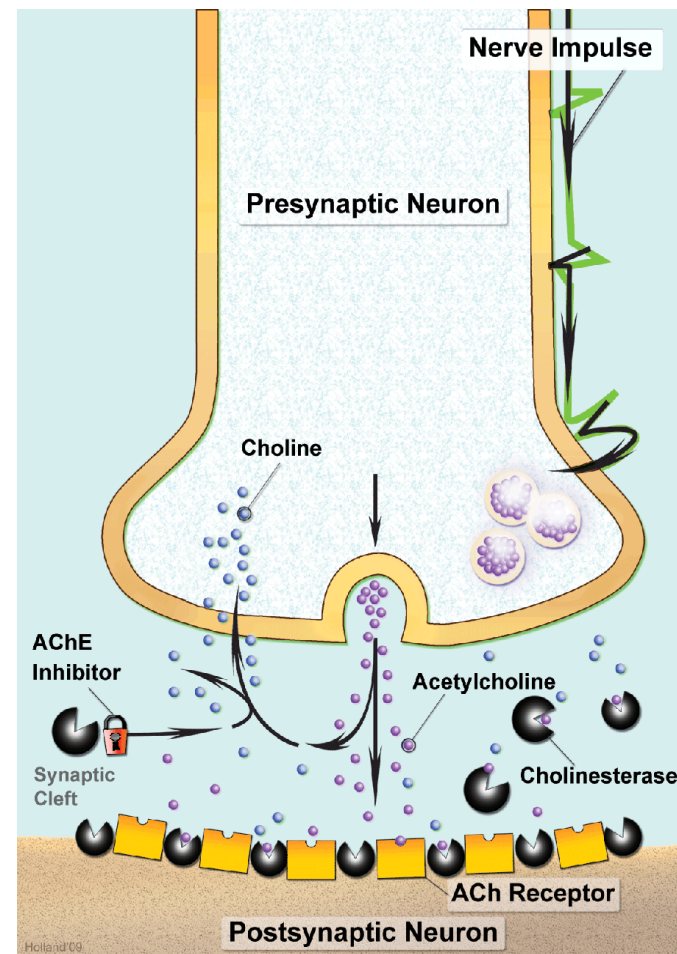
# Lessons Learned - Clinicians

- You are part of the public health system!
- Public health role
  - Recognize and define outbreak
  - Use data to drive prevention
- Rapid reporting from clinicians is critical
  - Report thru  
WA Poison Center**
- Clinicians need to identify pesticide for patient care and public health



# Why Did the System Work?

- Classic toxicology presentation – cholinesterase inhibition
- Confirmatory diagnostic tool



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# How Does EPA Know There Is a Problem with a Chemical

- Reports from **Clinicians**
  - These are rare- Clinicians don't know how to diagnose pesticide illness
- Surveillance data
  - State systems (For example: Washington)
  - NIOSH SENSOR system
    - Both dependent on **clinician reporting**
- Poison Control Data
  - Mostly Clinician reports are biased toward children and exposures not poisonings
- 6(a)2 reports from **Registrants**
  - Dependent on **clinician reports**



# What Tools Do We Have?

- Overexposure to Roundup?
- Overexposure to Pyrethroids?
- Overexposure to Atrazine?

# What about these Chemicals?

Newer targeted chemicals on the market

- Exterra (diflubenzuron)
  - chitin inhibition
- Spirotetramat (Movento)
  - ketoenole-inhibit lipid metabolism
- Spinosad (Success)
  - Nervous system excitation
- Imidocloprid (Admire)
  - Nicotine receptor stimulation



Images © PNASH

# Neonicotinoids

- Human data limited to 4 reports, -- 2 deaths of autopsy-confirmed imidacloprid poisoning
- Excess nicotinic stimulation
  - Disorientation, agitation, drowsiness, loss of consciousness, tachycardia
  - Rhabdomyolysis, V-tach/V-Fib in severe cases
- Diagnostics not available

Agarwal R, et al. Am J Emerg Med 2007;25:844-5

David D, et al, Clin Tox 2007;45:485-6

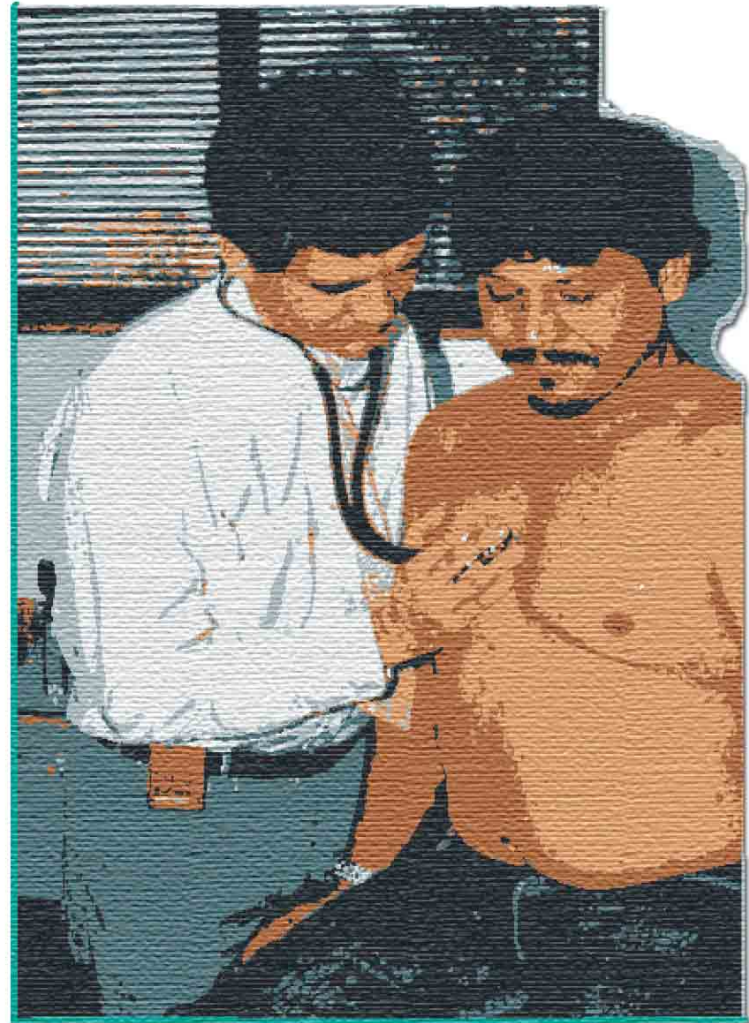
Huang NC, et al. Am J Emerg Med 2006;24:883-5

Wu IW, et al. J Tox clin Tox 2001;39:61 7-21.



# What Does a Clinician Face?

A farm worker complains of nausea, headache, weakness: got sick this morning while at work.



# Differential Diagnosis

Viral illness

Food poisoning

Hangover

Heat exhaustion

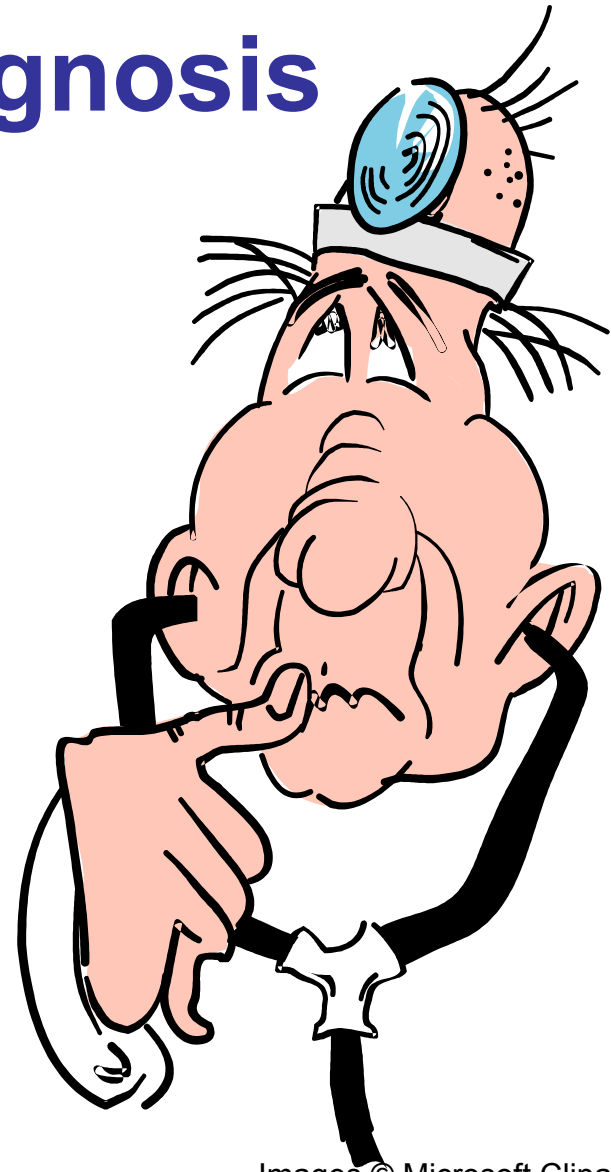
Medication reaction

Malaria

Pesticide poisoning

Green tobacco illness

Pregnancy (if female)





# What Tools Exist for Diagnosis

Condition	Diagnostic tools	Reliability
Viral illness	Various antigen tests	Excellent
Food poisoning	History only	Poor
Hangover	History and physical exam	Good
Heat exhaustion	History and exam	Good
Medication reaction	History	Average
Malaria	Blood smear	Excellent
Pesticide poisoning	History	Poor
Green tobacco illness	History and conitine	Excellent
Pregnancy if female	Exam and urine/blood	Excellent

# Clinical Tools for Diagnosing Pesticides?

- Cholinesterase Monitoring
  - Washington State
  - California



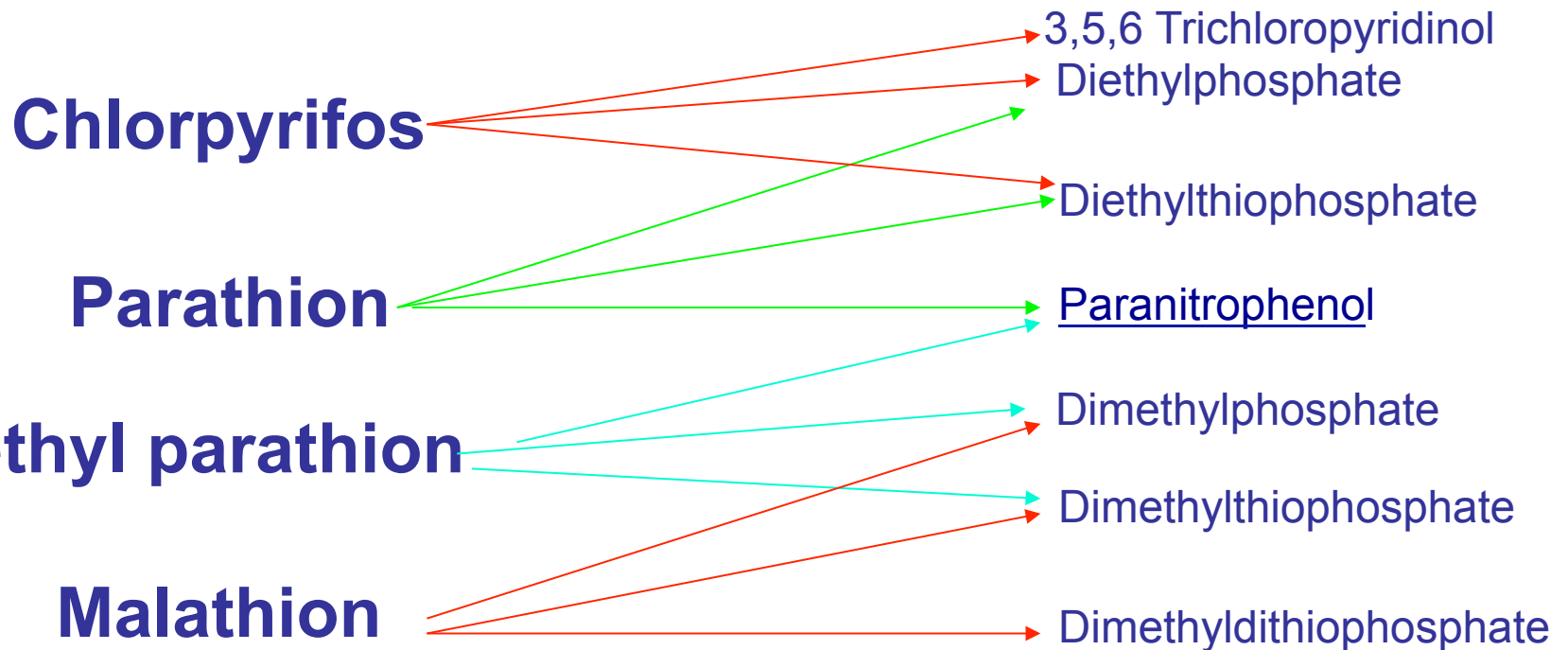
Images © PNASH



# Organophosphate Metabolites

(Found in Children's Urine)

No easily accessible tests for most pesticides







# Limited Diagnostic Tools for Clinicians



Images © Microsoft Clipart



# What Do We Treat?

- In most cases of pesticide overexposure decontamination and symptomatic therapy are indicated
- Antidotes exist for only:
  - Cholinesterase inhibitors-Atropine and 2-pam
  - Rodenticides- Fresh Frozen Plasma and Vit K
  - Cyanide containing pesticides
  - Force alkaline diuresis for some herbicides
  - Some you would not treat and
    - You want to know which not to treat

# Why Else Is It So Important?

- Workers' Compensation
- Specialty Care







## Worker Compensation and Agricultural Workers

- Not all ag workers are covered
- Those covered may not know/don't use
- They are usually the poorest of the poor
- They rarely have health insurance
- They use community clinics:
  - *That means federal dollars and no specialty care*
- Worker Comp may be their only insurance



## The Importance of Diagnosis in Workers' Compensation

“Accurate diagnosis is important with all disease, but with occupational disease it is even more so because of medicolegal implications. These implications make it essential that physicians use the most specific methods available to determine the degree of probability that a particular disease or injury has resulted from occupational exposure.”

**Guide to Diagnosis of Occupational Illness** *JAMA*. 1966;196(3):297-298.



## Objective Findings are “extremely important” in Work Related Illness

Objective findings are extremely important to claim managers in their decision-making process. You should be as specific and detailed as possible in describing objective findings to assure that the claim manager is able to make appropriate adjudicative decisions as expeditiously as possible and your patient receives the benefits to which he/she is entitled. (See Occupational



## **In Most Pesticide Overexposures**

- There is no objective evidence
- No objective evidence - No claim



# An Accurate Diagnosis Has Broad Implications

- An accurate diagnosis leads to care and prevention
  - For the worker
    - Appropriate Treatment
    - A reliable report to the Worker Compensation System
    - Removing worker from further exposure and worse illness
    - Education about how to avoid future overexposures
  - In the workplace
    - Correcting workplace hygiene failures
    - Notifying worker protection system for enforcement and prevention
  - For the Nation
    - Result in a report to a surveillance system
    - May result in systemic change through 6(a)2

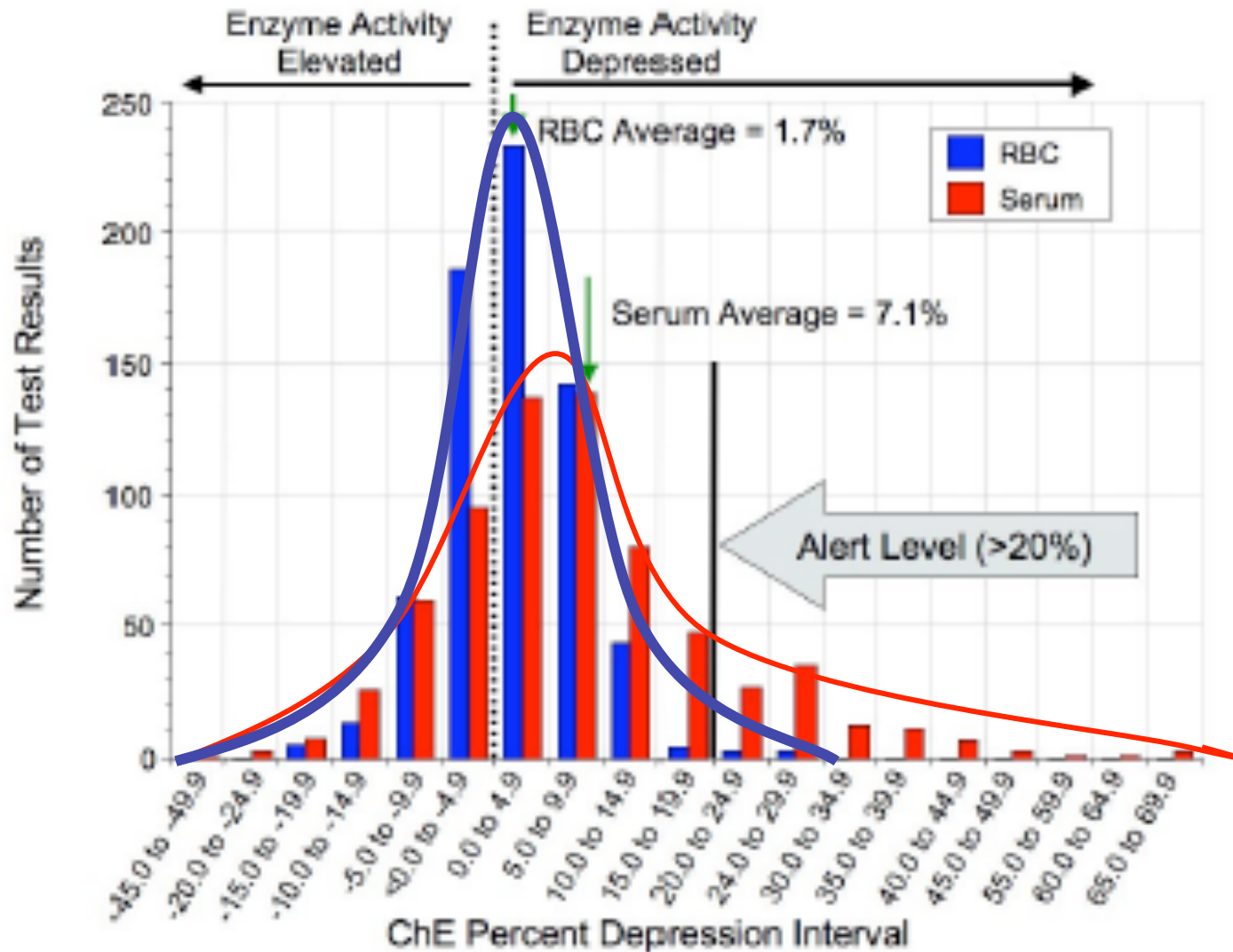
# Special Populations

- Pesticide poisonings present differently in children.
  - A seizure or pesticide poisoning?



Images © Alan Pogue

# ChE Monitoring in Washington State







# Incident Reporting Responsibility

## FIFRA 6(a)2

159.170

Information must be submitted which concerns any study that a person described in §159.158(a) has concluded, or might reasonably conclude, shows that a correlation may exist between exposure to a pesticide and observed adverse effects in humans. Information must also be submitted which concerns exposure monitoring studies that indicate higher levels of risk or exposure than would be expected based on previously available reports, data, or exposure estimates. Such information must be submitted regardless of whether the registrant considers any observed correlation or association to be significant.

159.184

- a) *General.* Information about incidents affecting humans or other non-target organisms must be submitted if the following three conditions are met:
- (1) The registrant is aware, or has been informed that a person or non-target organism may have been exposed to a pesticide.
  - (2) The registrant is aware, or has been informed that the person or non-target organism suffered a toxic or adverse effect, or may suffer a delayed or chronic adverse effect in the future.
  - (3) The registrant has or could obtain information concerning where the incident occurred, the pesticide or product involved, and the name of a person to contact regarding the incident.



# Diagnosis: The Weak Link





# HIPPA Exceptions

"(b) PUBLIC HEALTH.--Nothing in this part shall be construed to invalidate or limit the authority, power, or procedures established under any law providing for the reporting of disease or injury, child abuse, birth, or death, public health surveillance, or public health investigation or intervention.

"(c) STATE REGULATORY REPORTING.--Nothing in this part shall limit the ability of a State to require a health plan to report, or to provide access to, information for management audits, financial audits, program monitoring and evaluation, facility licensure or certification, or individual licensure or certification.



## The Link Weaker Still Health Insurance Privacy and Portability Act (HIPPA)

- What will this do to surveillance?
- You can't share privileged medical information without patient permission
- If You Do:

"(b) PENALTIES.--A person described in subsection (a) shall--

"(1) be fined not more than \$50,000, imprisoned not more than 1 year, or both;

"(2) if the offense is committed under false pretenses, be fined not more than \$100,000, imprisoned not more than 5 years, or both; and



# We Need Diagnostic Tests to Prevent Future Illness

- **The promise of biomonitoring**
  - The availability and application of biomonitoring or diagnostic tests permits the early identification of exposure induced illness before it becomes severe
  - This applies both to individuals and populations
  - In Short:
    - Identify individual illness in the preclinical state
    - Identify population illness in the pre-epidemic phase



## Epidemiological Studies Exposure Assessment Is the Weak Point

- “The substantial weak points of numerous epidemiological studies of pesticide-related health effects are **problems faced in exposure assessment**, small numbers of exposed subjects, a limited number of studies focused on the majority of cancers, and difficulties in estimating critical windows of exposure.”
- If we want good science, we must have markers for exposure.

*Int J Occup Med Environ Health. 2006;19(3):152-69. Exposure to pesticides and childhood cancer risk: has there been any progress in epidemiological studies? Jurewicz J, Hanke W.*



# Toxicity Testing in the 21st Century A Vision and a Strategy

Committee on Toxicity Testing and Assessment  
of Environmental Agents

*NATIONAL RESEARCH COUNCIL OF THE  
NATIONAL ACADEMIES*

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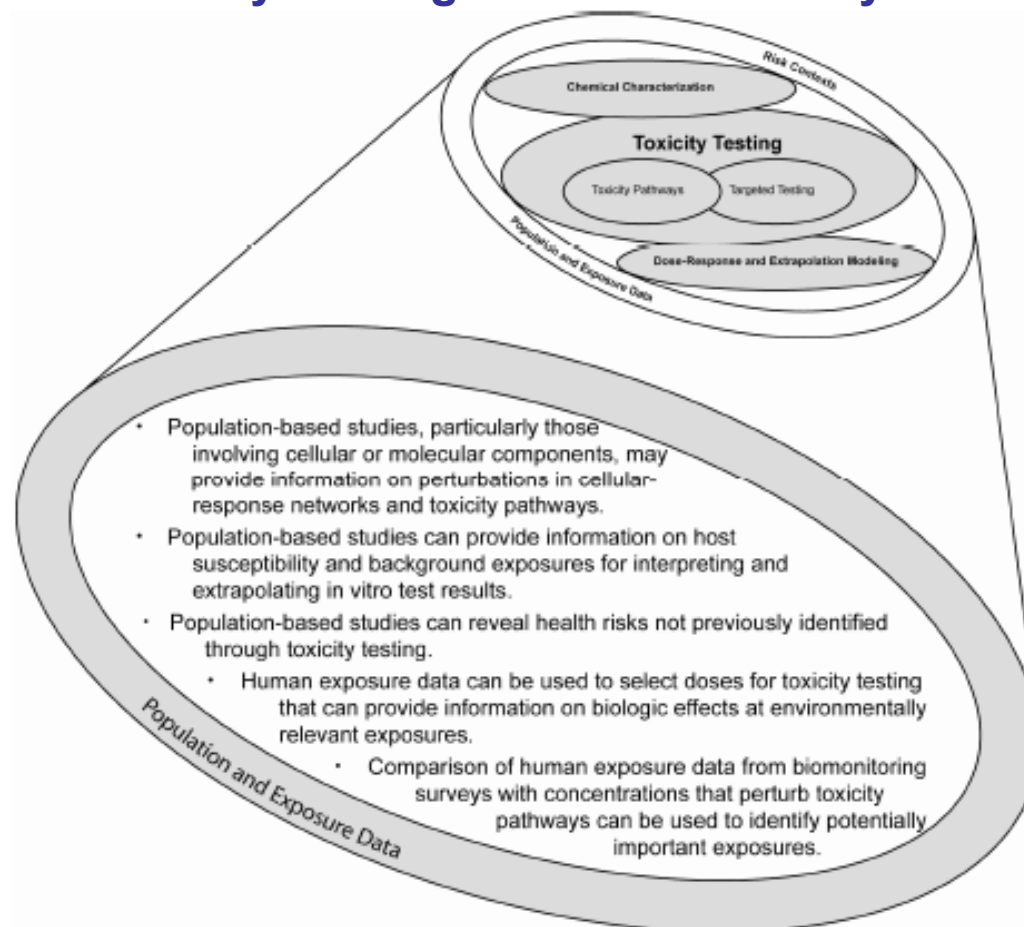


# Toxicity Testing in the 21st Century

## National Research Council

- Population based exposure data and biomonitoring are critical to success of the new paradigm
- Knowing what happens in the human population through biomonitoring and exposure assessment is the means of validating assumptions based on the new paradigm

## Population and Exposure Data, a Critical Component of the National Research Council Toxicity Testing in the 21<sup>st</sup> Century



**FIGURE 3-5** Overview of population-based and human exposure data component.



# Government Accountability Office Report, August 2009

GAO

United States Government Accountability Office  
Report to Congressional Requesters

April 2009

BIOMONITORING

EPA Needs to  
Coordinate Its  
Research Strategy and  
Clarify Its Authority to  
Obtain Biomonitoring  
Data



GAO-09-353



## What the GAO Found: EPA Made Limited Use of Biomonitoring Data in Risk Assessments

GAO recommends that EPA develop a comprehensive research strategy to improve its ability to use biomonitoring in its risk assessments; establish an interagency task force to coordinate federal biomonitoring research; and determine the extent of its legal authority to obtain biomonitoring data under TSCA, asking Congress for more authority if necessary. EPA agreed with the first two recommendations and did not disagree with the third, but provided substantive comments on its implementation.

- Addressed TSCA
- Did NOT address EPA's authority to require biomonitoring data under FIFRA
- FIFRA gives broad authority to the Administrator to require different kinds of data from a registrant



## Diagnosis with NEW Chemicals

- We need the tools because we don't know what the overexposure looks like.
  - In most cases information comes from ingestions in children or suicides
  - These are extreme and contaminated models
    - Dosages are very high
    - Children are different
    - Suicidal patients are not workers



# Why Do We Need Diagnostic Tests and Specific Biomarkers

- To improve clinical decision making
  - To initiate antidote use (if available)
  - To get workers the care they deserve (Worker Comp)
  - To make the workplace safer
  - To Improve training of clinicians in the diagnosis of overexposures
- To improve EPA's decision making
  - To enhance decisions regarding pesticides 6(a)2 and other surveillance systems
  - To protect human populations
  - To protect other exposed workers
- To monitor new chemicals and limit harm early
- To validate new toxicity testing paradigm
  - Part of the NRC vision for 21<sup>st</sup> cent Toxicity Testing
- To improve the science around the health effects of pesticides
  - Exposure assessment is the weakest link in environmental and occupational epidemiology



# Clinician's Role

- Identifying poisonings
- Treating patients
- Reporting poisonings
- Advocating for patients  
(workers)



# Clinicians Need Diagnostic Tools

- Frontline providers need these tools to deal with new chemicals and old.
- If we give clinicians a test, they can give you a diagnosis.



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**Pesticides are released into the worker's environment:**

**We need to know when they are in the worker's body**

- EPA fought to protect workers
- EPA won

## **1972 FIFRA Amendments**

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"There can be no question but that the bill (the Federal Environmental Pesticide Control Act of 1972) requires the Administrator to require that the labeling and classification of pesticides be such as to protect farmers, farm workers, and others coming in contact with pesticides or pesticide residues."

-- Senate Committee on Agriculture and Forestry



# Diagnostic Tests and Specific Biomarkers

Can the EPA the do it?

Under FIFRA they can!