

Effects of Pesticides on Children's Neurodevelopment



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Objectives

- To estimate sources, pathways and levels of ***in utero and postnatal pesticide exposures*** of children living in an agricultural community.
- To determine the relationship of pesticide exposure and:
 - **neurodevelopment**
 - growth
 - respiratory disease
- To reduce exposure of children to pesticides with **interventions and community outreach.**

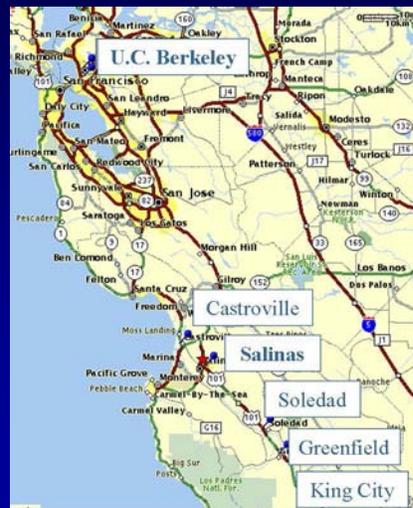
Organophosphates (OP)



- Widely used in agriculture
- Degrade quickly (hrs-days)
- Excreted in urine as dialkyl phosphate (DAP) metabolites
- Acute neurotoxins

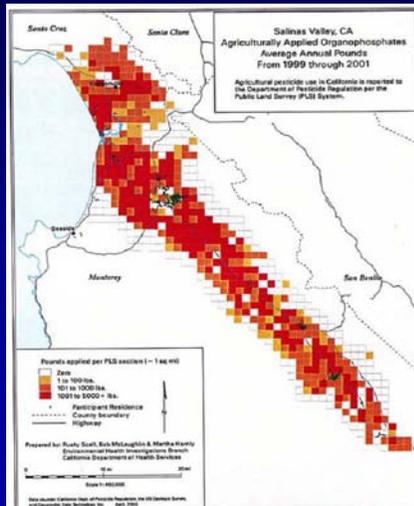


CHAMACOS Study Area





Pesticide Use in the Salinas Valley



500,000+ pounds of organophosphate pesticides used annually



Enrollment: 1999-2000

601 pregnant women who were living in Salinas Valley:

- Receiving prenatal care at Clinica de Salud del Valle de Salinas
- Less than 20 weeks gestation
- Medi-Cal eligible
- 18 years or older

CHAMACOS Biological Specimen Collection

	1 st Tri	2 nd Tri	Delivery	6 M	1 Y	2 Y	3½ Y	5 Y	7 Y
• Maternal Urine	ü	ü	ü	ü					
• Paternal Urine			ü						
• Maternal Blood		ü	ü						
• Cord Blood			ü						
• Breast Milk			ü	ü					
• Child Urine				ü	ü	ü	ü	ü	
• Child Blood					ü	ü		ü	ü
• Child Saliva							ü	ü	



High Retention Rates



	N	Retained
Delivery	538	
1Y	439	82%
2Y	412	94%
3½Y	365	89%
5Y	350	96%
7Y	352	101%

Pesticide Exposures



Organophosphate Pesticide Use in the Salinas Valley, 2001

OP Pesticide	Pounds	Excreted in urine as
Malathion	96,520	Dimethyl (DM) phosphates ~220,000 lbs. (42%)
Oxydemeton-methyl	57,859	
Dimethoate	34,224	
Naled	17,045	
Methidathion	14,220	Diethyl (DE) phosphates ~199,000 lbs. (38%)
Diazinon	133,537	
Chlorpyrifos	54,945	
Disulfoton	10,216	Other ~104,000 lbs. (20%)
Acephate	71,725	
Bensulide	32,669	
Total	~520,000	



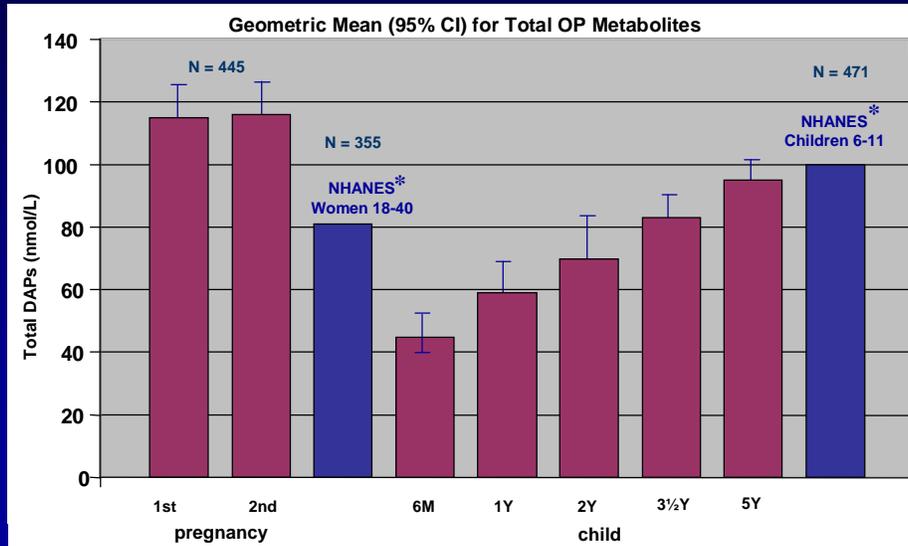
OP agricultural pesticide use before and after US residential ban

Pesticide	Lbs per year							
	1999	2000	2001	2002	2003	2004	2005	2006
Diazinon	104,000	122,000	134,000	143,000	159,000	172,000	158,000	145,000
Chlorpyrifos	63,000	55,000	55,000	53,000	58,000	61,000	66,000	62,000

**Residential
Ban**

All CHAMACOS children were born after the residential ban

Prenatal and child OP metabolites in CHAMACOS and National Reference*



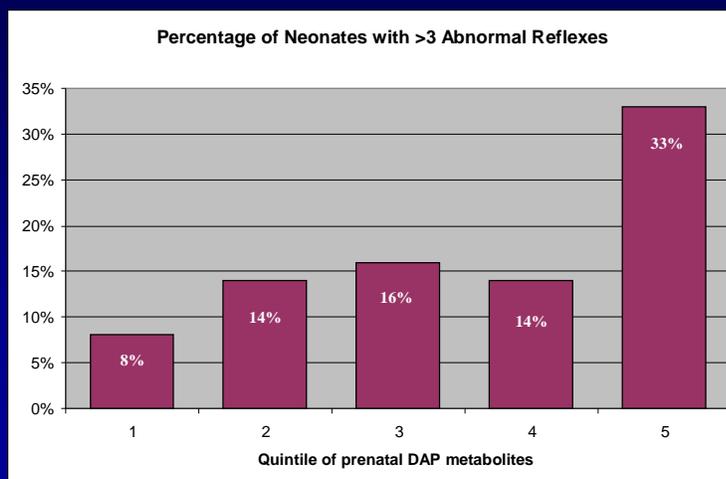
* National Health and Examination Survey

Bradman et al., 2005

Do these pesticide exposures affect children's neurodevelopment?

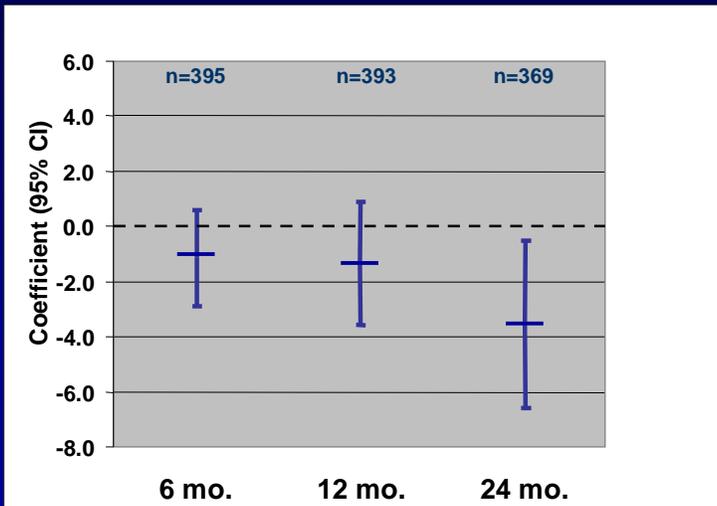


Higher Prenatal OP Exposure is Associated with Abnormal Reflexes in Neonates (n=184)



C^2_{trend} 6.7
P value 0.01

Prenatal DAPs and Bayley Mental at 6, 12, and 24 months

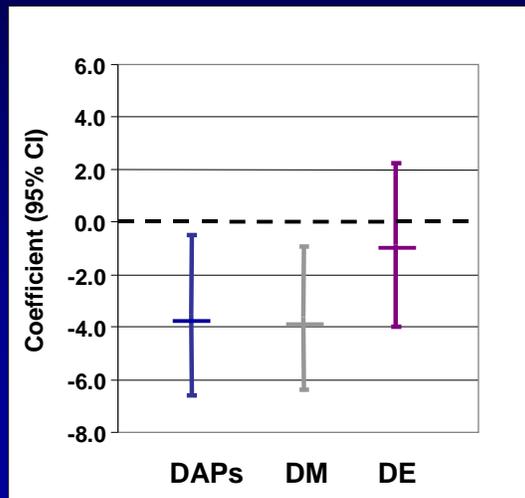


* All models adjusted for psychometrician, gender, age, parity, assessment location, breastfeeding duration, maternal PPVT, poverty status, and HOME score.

Eskenazi *et al.*, 2007



Total DAPs, DMs, and DEs and 24-month Bayley Mental



* All models adjusted for psychometrician, gender, age, parity, assessment location, breastfeeding duration, maternal PPVT, poverty status, and HOME score.

Eskenazi *et al.*, 2007

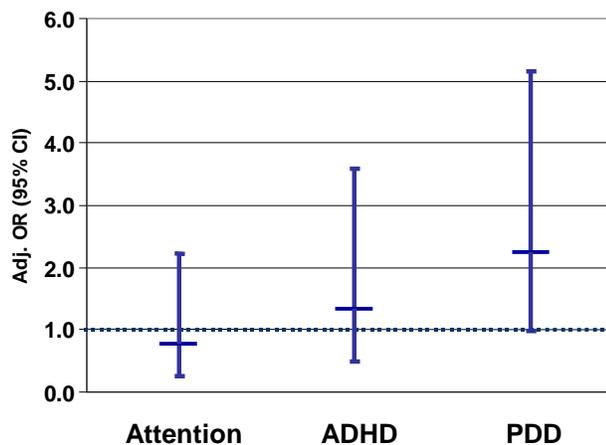
Child Behavior Checklist 1½ - 5 year old DSM-Oriented Scale

Pervasive Developmental Disorder

- Afraid to try new things
- Avoids looking others in the eye
- Can't stand having things out of place
- Disturbed by any change in routine
- Doesn't answer when people talk to him/her
- Doesn't get along well with other children
- Repeatedly rocks head or body
- Shows little affection towards people
- Speech problem (describe)
- Strange behavior (describe)
- Upset by new people or situations (describe)
- Withdrawn, doesn't get involved with others



Prenatal DAPs and 24-month Child Behavior Checklist (Adj.* OR)

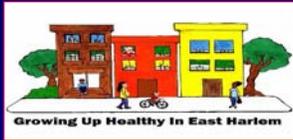


* All models adjusted for gender, parity, duration breastfed, maternal PPVT, poverty status, HOME score, and maternal depression.

Attention and ADHD scales use borderline (>93rd percentile) cutpoint;
PDD scale uses clinical (>98th percentile) cutpoint

Eskenazi et al., 2007

Comparison of Findings with Other Studies



Mary Wolff, Stephanie Engel, Gertrud Berkowitz
Mount Sinai School of Medicine

Virginia Rauh, Robin Wyatt, Frederica Perera
Columbia University



Brenda Eskenazi, Kim Harley, Asa Bradman, Amy Marks
University of California, Berkeley

Biomarkers of Prenatal OP Pesticide Exposures

	In Urine	In Blood
	Dialkyl Phosphates (DAPs)	Chlorpyrifos (CPF)
Berkeley	X	
Mt. Sinai	X	
Columbia		X

Early Childhood Neurodevelopmental Outcomes

	Brazelton	Bayley				WPPSI	
	Neonatal	6M	1Y	2Y	3Y	3.5Y	5Y
Berkeley	X	X	X	X		X	X*
Mt. Sinai	X		X	X			
Columbia			X	X	X		X

* Verbal IQ assessed with PPVT

Early Childhood Behavioral Outcomes

	Child Behavior Checklist (CBCL)		
	2Y	3Y	3.5Y
Berkeley	X		X
Mt. Sinai			
Columbia		X	

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URBAN NEW YORK

Demographics of Study Populations

	Berkeley (%)	Mt. Sinai (%)	Columbia (%)
Race/Ethnicity			
Non-Hispanic White	1	20	--
African-American	--	27	35
Hispanic	Mexican 97	Mex, PR 51	Dominican 65
Other	2	1	--
Married	82	29	29
< High school	81	32	35

Associations with 7 Brazelton Clusters

DAPs

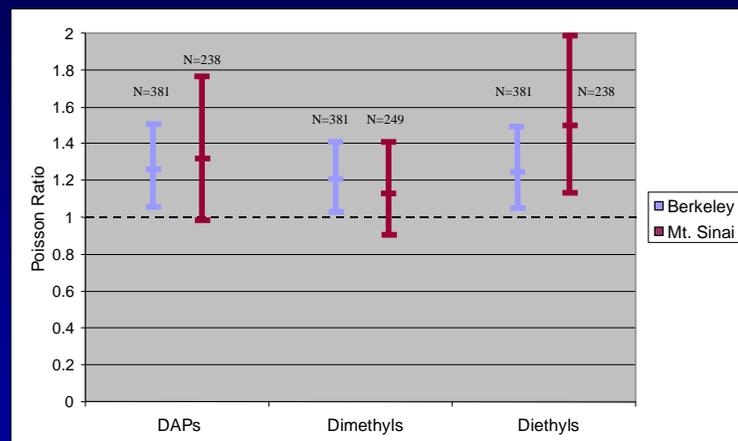
Berkeley 6/7 No associations

Mt Sinai 6/7 No associations

EXCEPT....

Young *et al.* 2005; Engel *et al.* 2007

Association between DAPs and Brazelton reflexes in both cohorts



Young *et al.* 2005; Engel *et al.* 2007

Prenatal OPs and Bayley Mental Development Index

	Berkeley (Log ₁₀ DAPs) Adj b	Mt. Sinai (Log ₁₀ DAPs) Adj b	Columbia (High v. Low CPF) Adj b
6 Months	-1.2		--
1 Year	-1.3		-0.3
2 Years	-3.5**		-1.5
3 Years	--		-3.3*

* p < 0.1; ** p < 0.05

Eskenazi *et al.* 2007; Rauh *et al.* 2006

In summary...

- Three scientifically-rigorous, cohort studies
 - Different populations
 - Different exposure levels and sources
 - Exposure measured using biomarkers in urine (metabolites) and blood (parent compound)
- Despite these differences, some patterns emerge...

In summary...

- Prenatal OP exposure associated with:
 - Increased odds of abnormal reflexes in neonates
 - Poorer mental development in 2 and 3 year olds
 - Increased odds of pervasive developmental disorder



Investigators

Health Studies

- Brenda Eskenazi
- Ira Tager
- Kim Harley
- Laura Fenster, DHS
- Caroline Johnson
- Michael Lipsett, DHS
- Janet Macher, DHS

Exposure Studies

- Asa Bradman
- Tom McKone
- Dana Barr CDC
- Rosemary Castorina
- Martha Harnly, DHS
- Jim Leckie, Stanford
- Marcia Nishioka, Batelle
- Jackie Schwartz

Mechanism Studies

- Nina Holland
- John Casida

Biostatistical Core

- Nick Jewell
- Alan Hubbard
- Amy Marks

Intervention and Community Outreach

- Abbey Alkon, UCSF
- Lisa Goldman
- Alicia Salvatore
- Jorge Hernandez Clinica

Clinica de Salud

- Jacki Sedgwick
- Max Cuevas

Natividad Medical Center

- Marc Tunzi

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