



Children's Health and the Environment: the American Experience

Brenda Eskenazi, PhD
Center for Environmental Research and Children's Health
School of Public Health
University of California, Berkeley



IEA-WCE Symposium
August 20, 2017



1



October 2010



US Collaborative Perinatal Project 1959-1965



Affiliated Institutions



- Established in 1951 by Congress to address maternal and infant mortality and cerebral palsy
- 60,000 pregnancies enrolled with 58,000 live born infants from 12 university hospitals

Hardy, Annals of Epi, 2003



3

US Child Health and Development Studies 1959-1967

- Recruited pregnant Kaiser Health Plan members in Oakland, California
- 20,000 pregnancies with 17,000 children at 5-year contact



chds
Child Health and
Development Studies

van den Berg, Paed Peri Epi, 1998



4

Strengths of these early cohort studies

- Collected serum samples (maternal and cord) from large number of participants.
- Numerous publications
- Excellent retention
- For subsamples of cohorts (CHDS), 4 generation follow-up



5



CPP

COLLABORATIVE PERINATAL PROJECT

Key weaknesses of the CPP

- Convenience sampling
- 12 recruiting institutions
- Inefficient and expensive due to number of collaborators and inadequate leadership
- Lack of cooperation among institutions
- Lack of trust between directors and staff
- Lack of commitment to CPP
- Did not collect data on maternal prenatal alcohol consumption
- Early failure to produce & publish results
- Termination of follow-up in 1976

Hardy, Annals of Epi, 2003



6



Key weaknesses of the CHDS

- Limited generalizability; sample limited to Kaiser members in Oakland
- Only sera collected; Placentas discarded
- Difficult to support the ongoing effort for generations

Both studies tell us little about modern day exposures, medical practices, or epidemics.

van den Berg, Paed Peri Epi, 1988



7



HEALTH GROWTH ENVIRONMENT

The National Children's Study (<2009-2014)

- Authorized by Congress (Children's Health Act of 2000)
- Proposed a nationally representative longitudinal cohort study of 100,000 followed from birth to age 21
- Aimed to assess the effects of environmental exposures (chemical, biological, physical, psychosocial) and gene-environment interactions on pregnancy outcomes, child health and development, and precursors of adult disease



8

The Demise of the US National Children's Study

Pilot study launched in January 2009, data collected on 6,000 families *but it failed*. **WHY?**

- Poor leadership and inflexible management structure
- Unrealistic study design
- Escalating costs of data collection and costly decisions:
 - Plan to enroll ~25% of the cohort before pregnancy
 - Plan to recruit families door-to-door

*NIH stopped data collection in December 2014 with more than **one billion dollars invested**.*



Landrigan & Baker, NEJM, 2015; NCS Working Group Report, 2014; Duncan, JAMA Ped, 2015

ECHO like Phoenix rises from the ashes



ECHO

Environmental influences
on Child Health Outcomes

A program supported by the NIH



ECHO'S PROGRAM OBJECTIVES:



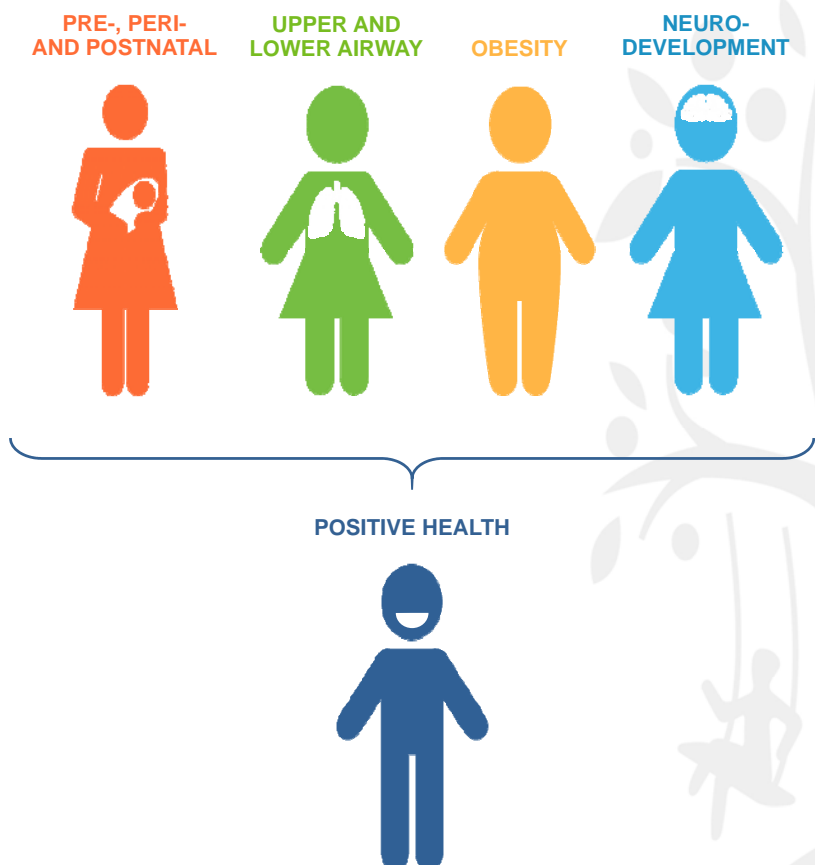
- Improve the health of children and adolescents by conducting **observational and intervention research** that will inform high-impact programs, policies, and practices.
- Institute best practices for conducting Team Science in the 21st century, giving researchers the tools to **work collaboratively** to improve child health.

ECHO'S OVERARCHING SCIENTIFIC GOAL:

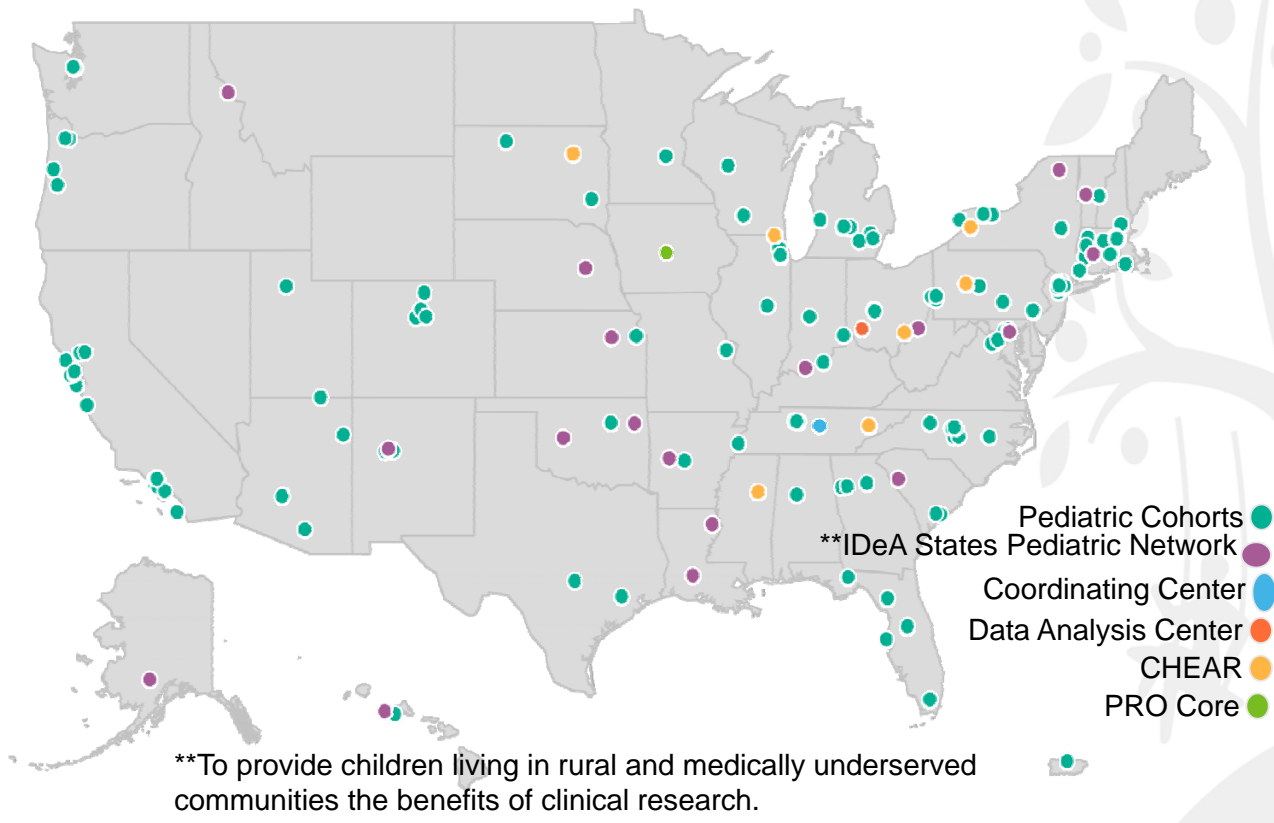
- Answer crucial questions about the effects of a **BROAD** range of **EARLY** environmental influences on child health and development

ECHO's health outcomes

Focus on key pediatric outcomes that have a high public health impact



ECHO is Nationwide: 44 States + DC +PR



Create the ECHO-wide cohort

- Start with 84 existing cohorts of mothers and children
 - Follow the children longitudinally
- Cohorts contribute to a single data platform to conduct solution-oriented observational research
 - Harmonize existing measures
 - Standardize new measures
- Goal >50,000 children
- A national research resource for use by ECHO investigators and others

ECHO's Unique Challenges



- Unifying data collection moving forward
- Data sharing
- Conducting statistical analyses with disparate populations



15

Unique Challenges for a U.S. Birth Cohort



- Cultural, language and demographic heterogeneity
- Protection of the individual vs. society
- Health care system not unified yet
- Widespread geographic areas; mobility
- Family structure



16

Are there advantages of smaller birth cohorts ?

*“Ensuring adequate representation of **our nation’s most disadvantaged children in [national] studies ... is a formidable task...”***

-Duncan, JAMA Ped, 2015

Birth cohort studies focused on select populations may provide important data on disadvantaged or unique populations that would be “washed out” in national studies.



17

Center for the Health Assessment of Mothers and Children of Salinas



**CENTER FOR THE HEALTH ASSESSMENT OF
MOTHERS AND CHILDREN OF SALINAS**

A birth cohort study investigating the health effects of environmental exposures in low income Mexican-American children living in an agricultural community



18

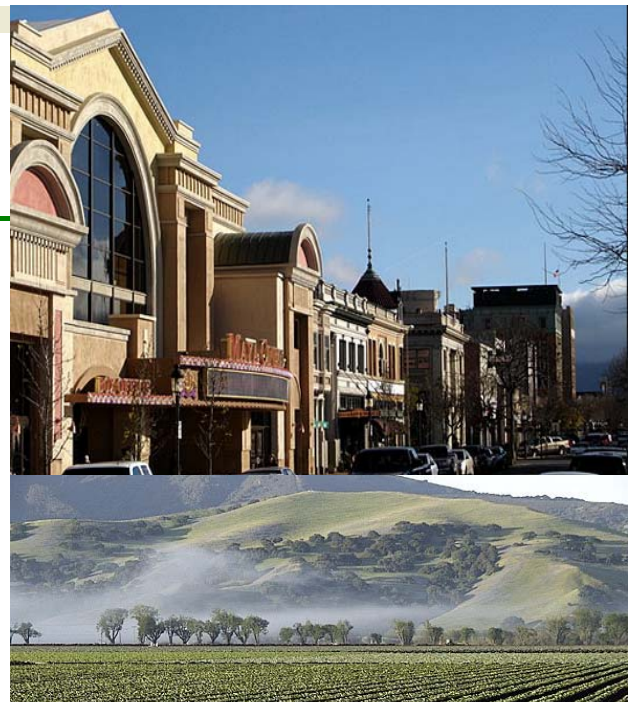
Salinas Valley

The “Salad Bowl” of the Nation



Salinas (pop 150K) Salinas Valley, Monterey

- 75% Latino, mostly Mexican
- 31% below the poverty level
- 2.5 X homicides than US average
- 10% HS students report being in gang



Salinas is one of six high-risk communities nationally for youth gang violence and, alongside cities such as Detroit and Inglewood in Los Angeles, as having one of the highest gang-related homicide rates in the U.S.

- U.S. Dept of Justice-led National Forum on Youth Violence Prevention



In 1999-2000, we enrolled 601 pregnant women from clinics serving farm workers

- 92% Spanish-speaking
- 85% born in Mexico
- 54% < 5 years in U.S.
- 96% living within 200% of poverty
- 44% 6th grade education or less
- 44% worked in agriculture during pregnancy
- 84% other agricultural workers in home

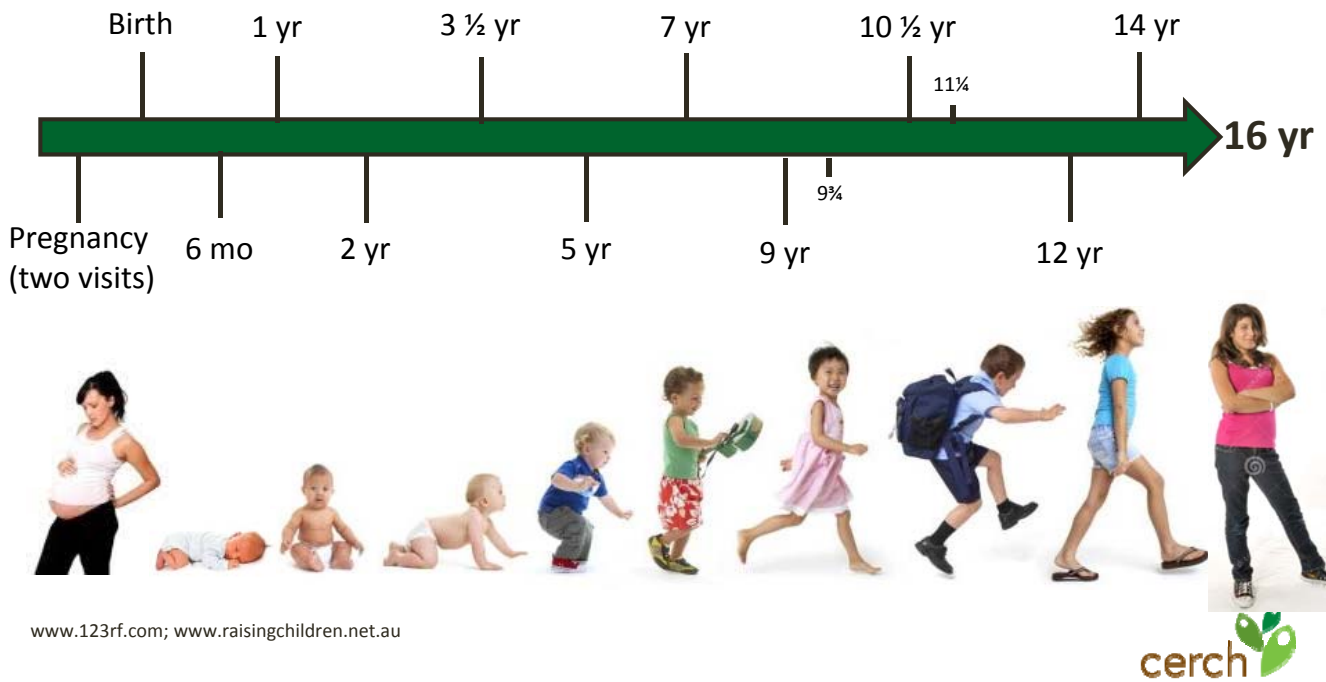


CHAMACOS is...

- A community-based participatory research project
- Studying the impact of environmental chemicals on farmworker families
 - Growth: fetal and child
 - Neurobehavioral development
 - Respiratory disease
 - Pubertal onset
- Exposure studies
- Mechanistic studies
- Community outreach and translation activities



CHAMACOS is a longitudinal birth cohort study (N=600-900)



We followed the children...
They are 16 years old now!

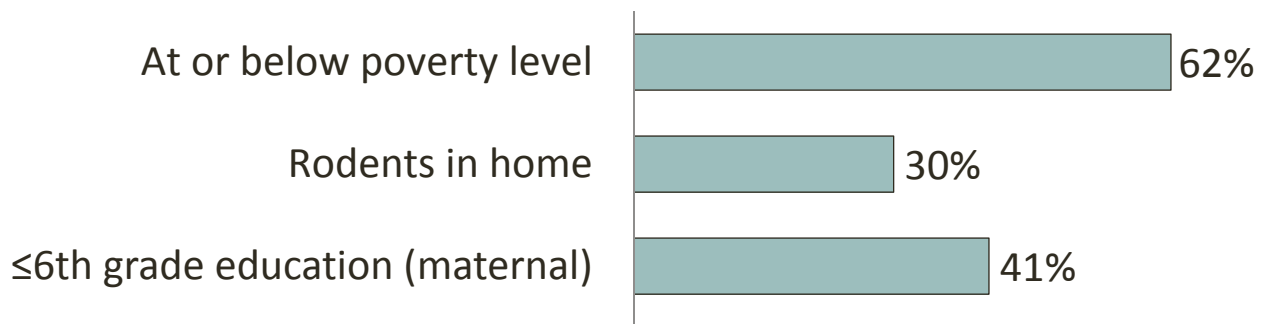
	1 st Tri	2 nd Tri	Delivery	6M	1Y	2Y	3½ Y	5Y	7Y	9Y	10½Y	12Y	14Y
Maternal Questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Physical Exam			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Neurodevelopment Assessment			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Home Inspection	✓			✓	✓	✓	✓	✓					
Lung Function Tests								✓	✓				
School Performance									✓	✓			
Tanner Stage										✓	✓	✓	✓

CHAMACOS Biological Specimen Collection

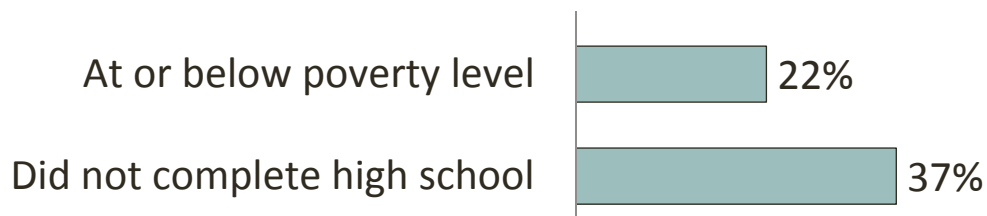
	1 st Tri	2 nd Tri	Delivery	6M	1Y	2Y	3½ Y	5Y	7Y	9Y	10½Y	12Y
Maternal Urine	✓	✓	✓	✓								
Paternal Urine			✓		Over 250,000 Stored Samples							
Maternal Blood		✓	✓							✓		
Cord Blood			✓									
Breast Milk			✓	✓								
Child Urine				✓	✓	✓	✓	✓		✓		
Child Blood					✓	✓		✓	✓	✓		✓
Child Teeth									✓	✓	✓	
Child Saliva							✓	✓				
Child Hair											✓	
House Dust	✓			✓	✓							

Adversity during pregnancy: CHAMACOS cohort

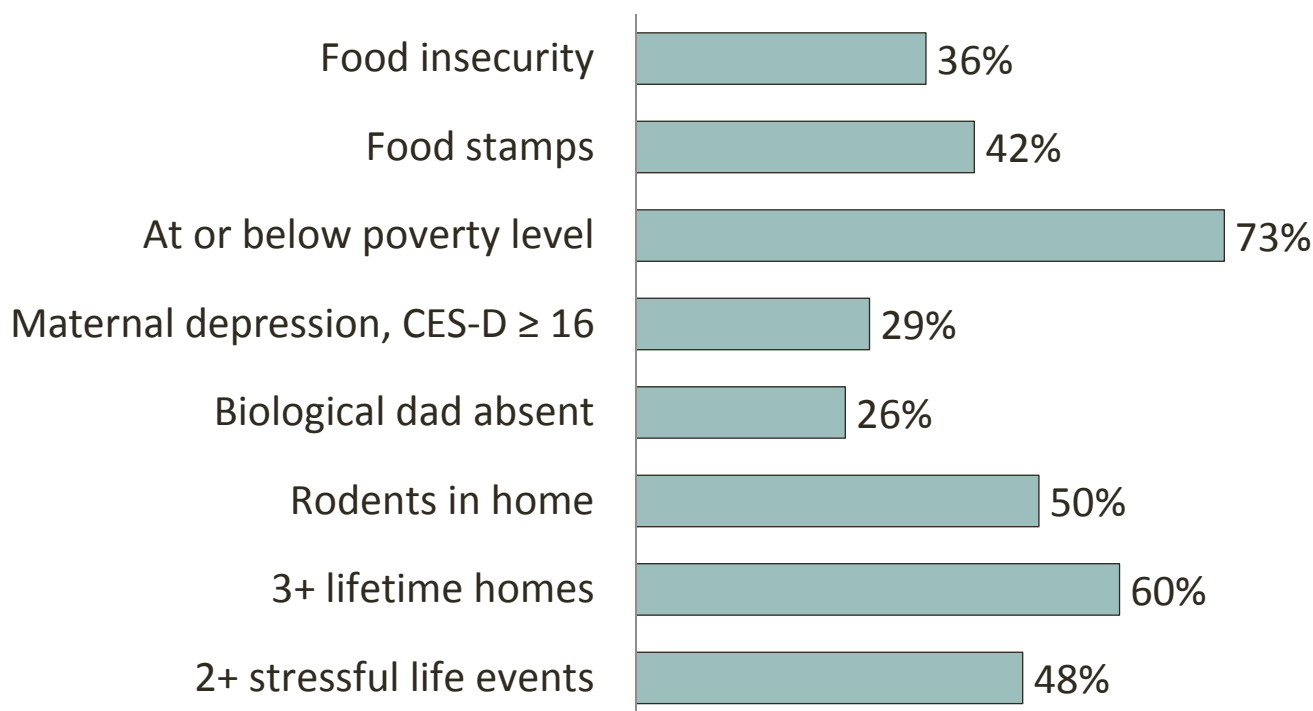
Individual-level



Census-tract level



Adversity at 7-9 years: CHAMACOS cohort



Chemical Exposures of Interest

We have measured about 100 chemicals

- Pesticides:
 - Organophosphates (OPs)
 - Pyrethroids
 - Methyl bromide
 - Fungicides containing manganese
 - Organochlorines, e.g. DDT
- Flame retardants (PBDEs) and newer chemicals
- Chemicals in plastics e.g. Bisphenol-A (BPA), Phthalates
- Air pollution

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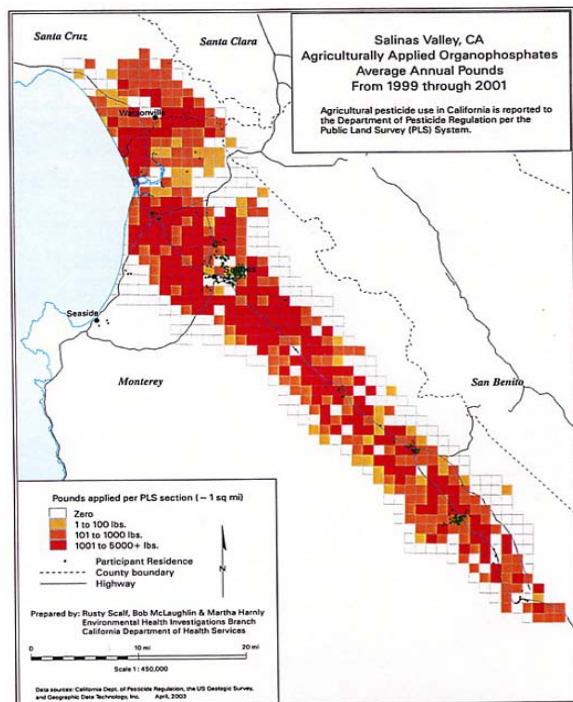
Organophosphate (OP) Pesticides



- Acute neurotoxins
- Depress AChE, causes CNS over-excitation
- Widely used in homes before 2001
 - 2001: Chlorpyrifos removed
 - 2004: Diazinon removed
- Account for ~35% of all insecticides used
 - >30 million lbs used per year
- Degrade quickly (hrs-days)
- Excreted in urine as dialkyl phosphate (DAF metabolites)



OP Pesticide Use in the Salinas Valley



500,000+ pounds of organophosphate pesticides used annually



DAPs: Prenatal Biomarker of OP Pesticide Exposure

- Urine samples from pregnant mother's at ~ 13 and 26 weeks gestation
- Measured dialkylphosphate metabolites (**DAPs**) as a biomarker of exposure to organophosphate pesticides



We found OP pesticides in:



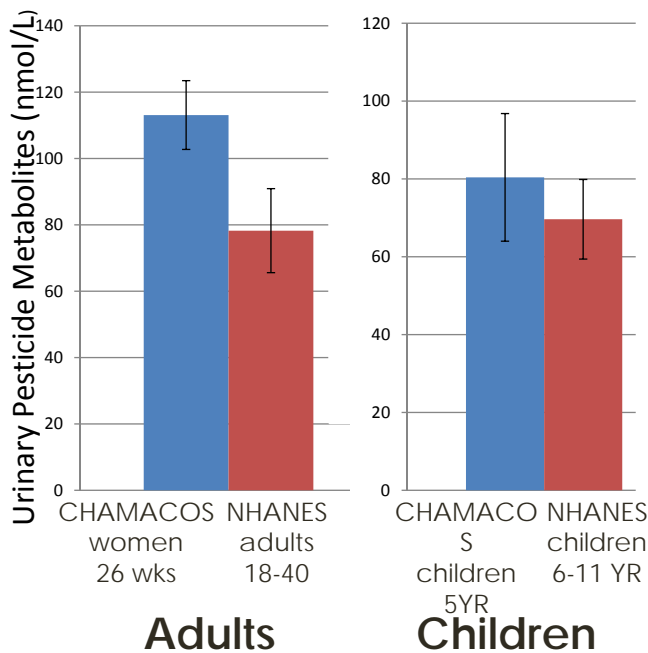
House dust



Breast milk 

Harnley et al., ES&T, 2009
Weldon et al., J Environ Mon 2011

CHAMACOS participants' OP metabolites are high compared to US



Bradman et al. EHP, 2005, 2011

Mom's OP pesticide metabolites during pregnancy were associated with:

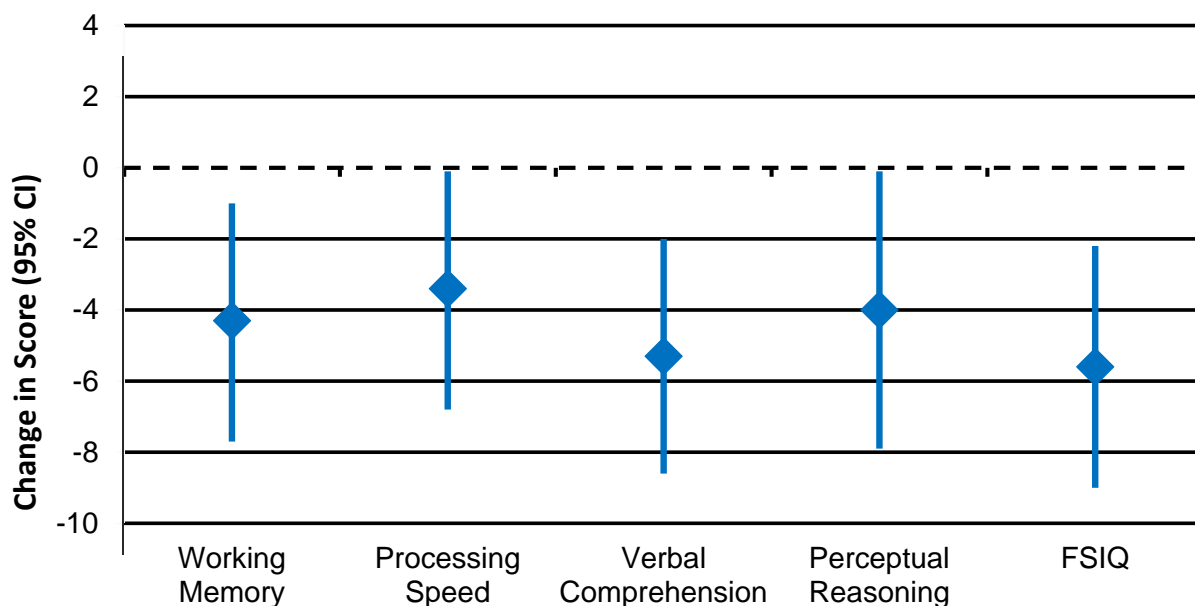


- Shortened gestation
- Abnormal neonatal reflexes
- Decreased mental development in toddlers
- Poorer verbal abilities in preschool
- Pervasive Development Disorder (Autism-like behaviors)
- Attention problems in school-age

Eskenazi et al., EHP, 2004; Young et al., Neurotoxicology, 2005; Eskenazi et al., EHP, 2007; Marks et al., EHP, 2010



Prenatal OP metabolites related to decreased WISC Scores at 7 years (n=312)



Adjusted for child's age, sex, language of assessment, maternal education, maternal intelligence, household poverty level, maternal depression, maternal country of birth and HOME score.

Bouchard et al., EHP 2011



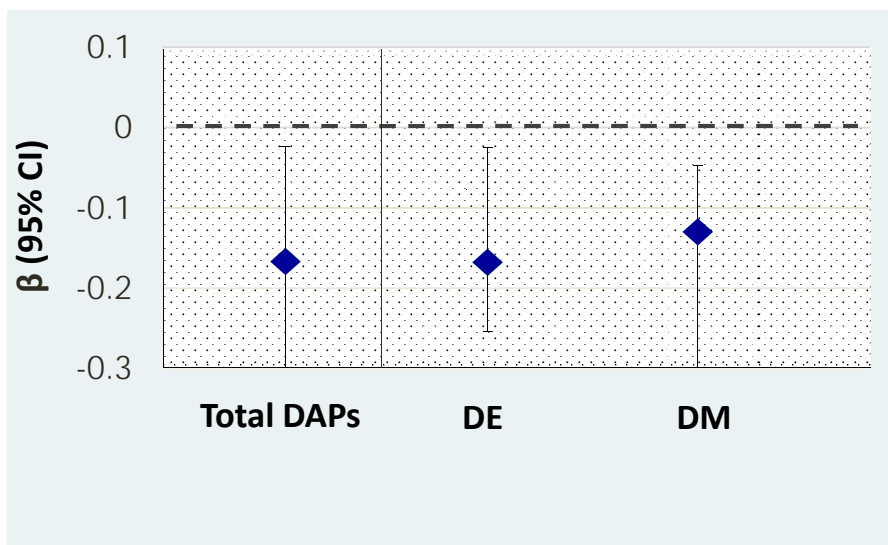
OP pesticide exposure and asthma



- Acute OP pesticide exposure associated with respiratory distress
- Some occupational studies show association of OP exposure and poorer respiratory outcomes
- Parasympathetic nervous system controls of lung tissue



Postnatal DAPs exposure associated with FEV1 at age 7 n=207



Adjusted for:
Child's gender
Child's age
Maternal smoking
ETS
Season of birth
PM2.5
Breastfeeding
Mold
Traffic
Roaches



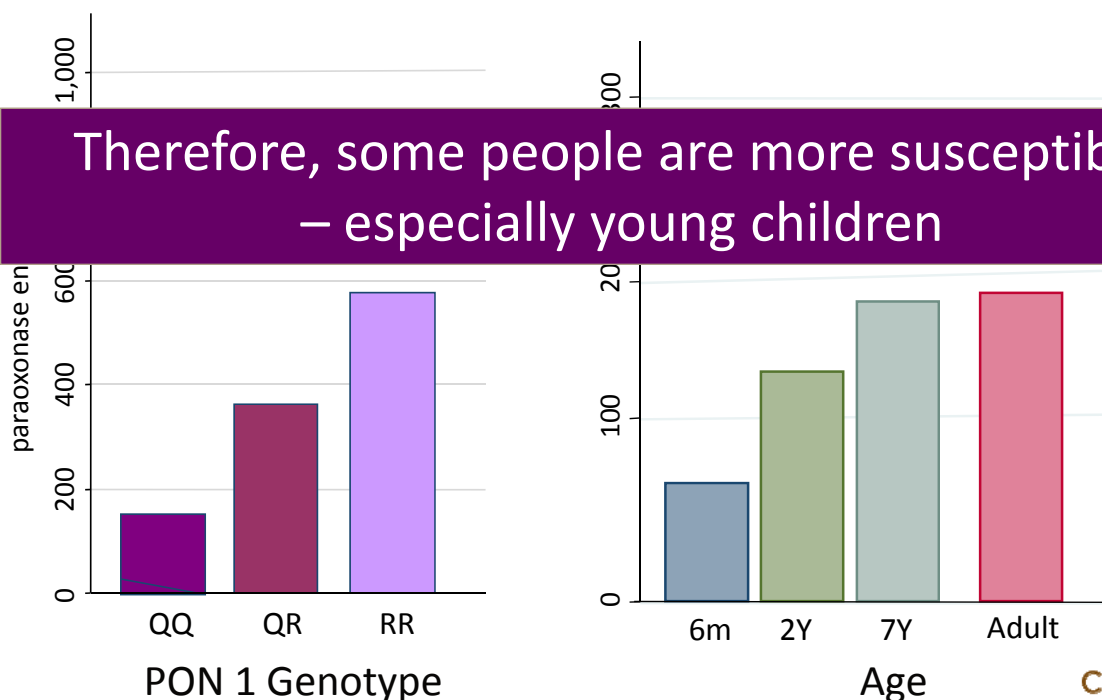
Are there some who are more susceptible to OPs?



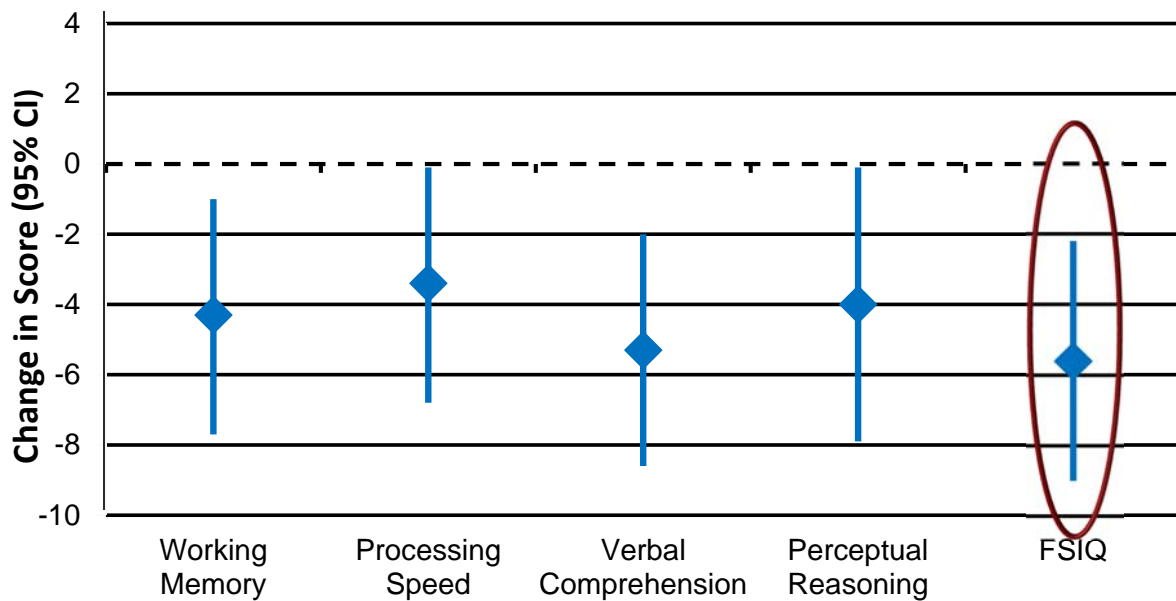
- Paraoxonase enzyme detoxifies OPs in the body
- Amount and efficiency of the enzymes depend on genes called PON1



The levels and efficiency of enzymes depends on your genetics ...and your age



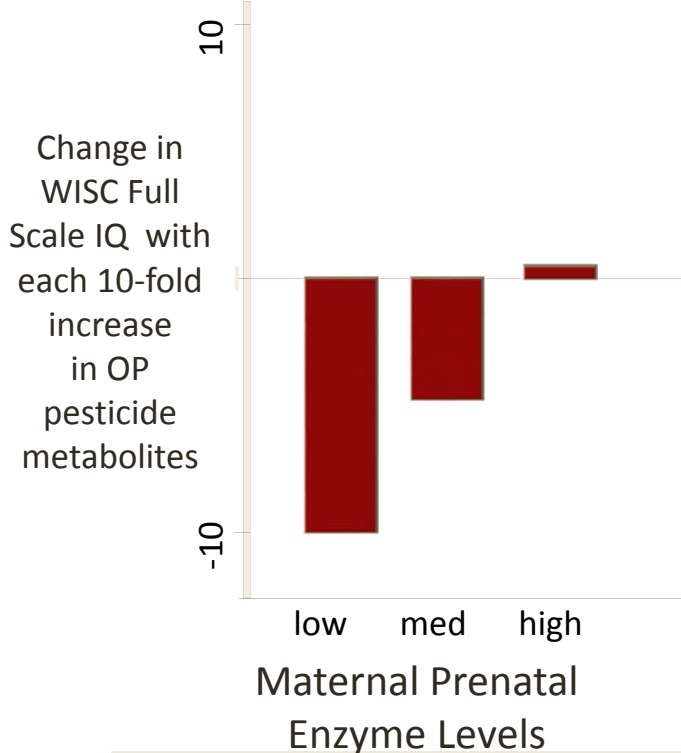
Prenatal OP metabolites related to decreased WISC Scores at 7 years (n=312)



Bouchard et al., EHP 2011



Mom's OP metabolites related to poorer children's IQ especially in moms with lower PON enzyme



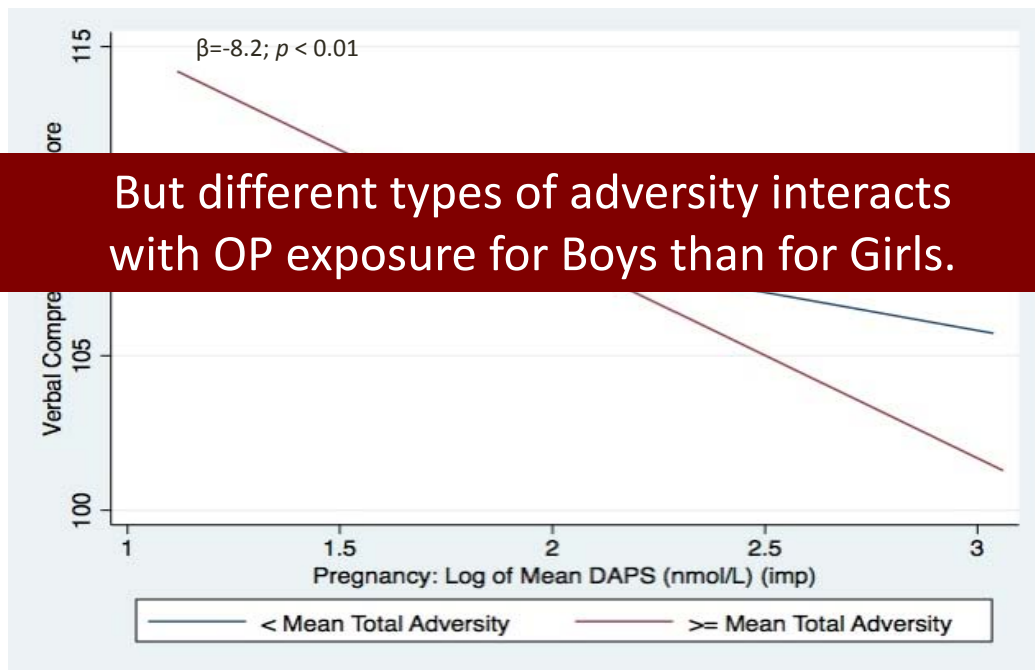
Collegeforlatinos.com

*Adjusted for maternal education, maternal IQ, HOME score at 6 months, and maternal PON192 genotype plus language of assessment.

Eskenazi et al., Environmental Research 2014



Interaction Between Adversity and DAPs on 7y IQ



But different types of adversity interacts with OP exposure for Boys than for Girls.

Model adjusted for maternal IQ score and language of neurological assessment.

Stein et al., 2016



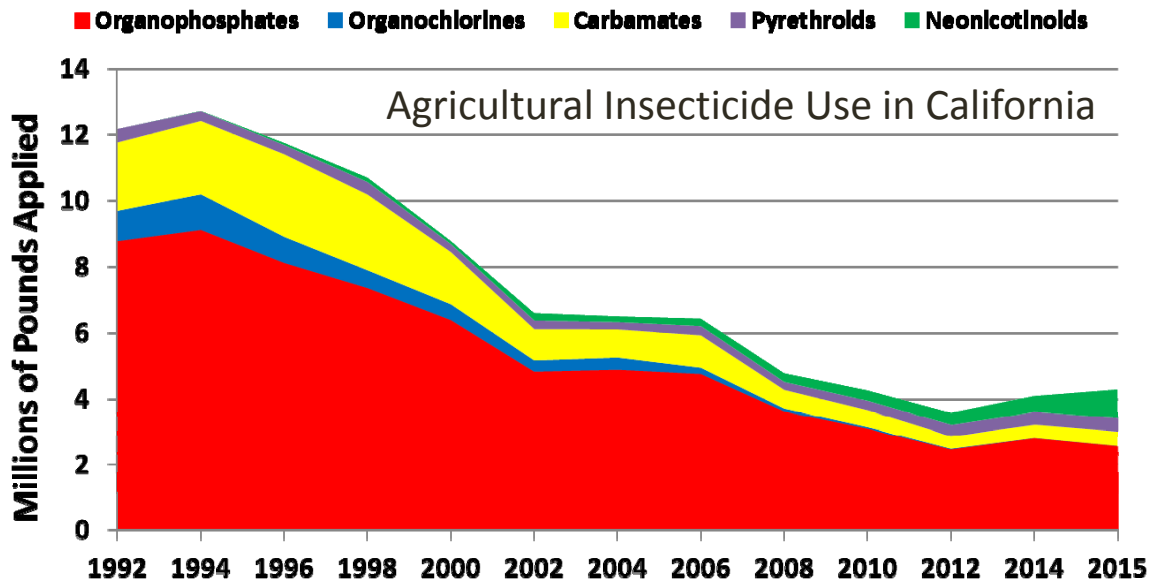
Neurotoxic exposome



Neurobiology/genetics



Our work on this small birth cohort has informed regulators

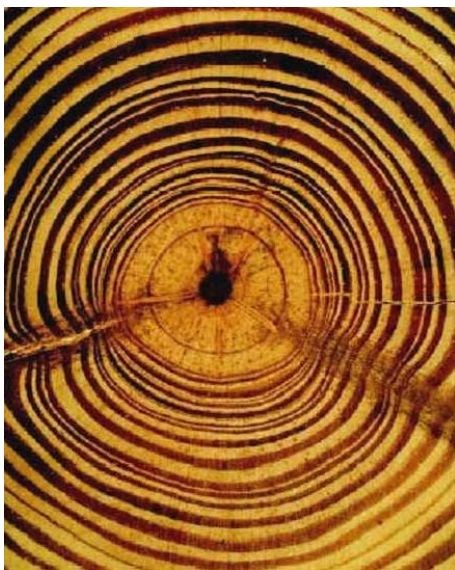


Source: California Department of Pesticide Regulation, 2013

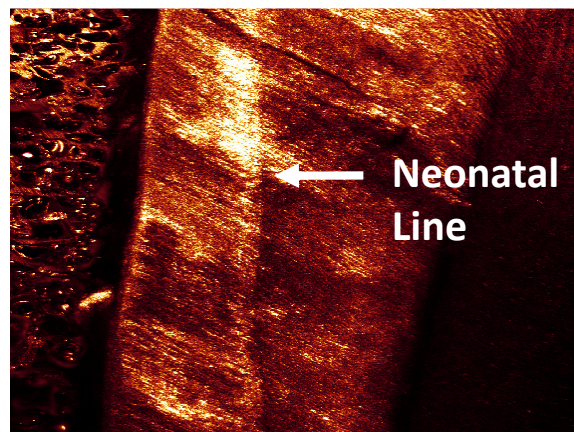


Our work has also helped to develop new exposure science.

Growth rings in a tree



Growth rings in teeth



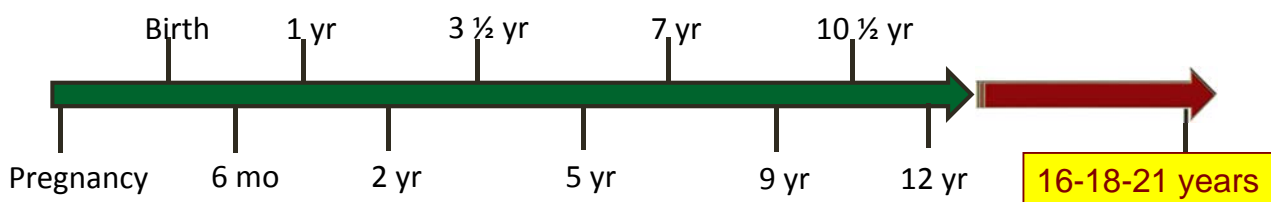
Arora et al., Environ Sci Tech, 2012;
Austin et al., Nature, 2013



Developed educational programs for the entire community.



We will continue to follow CHAMACOS into *adulthood!*



And of the next generation...



Many lessons have been learned...

- Engage the community
- Process blood samples for multiple types
- Never use the last aliquot; make sure you have small aliquots
- Collect as many different biological samples (e.g. fecal, teeth)
- Collect extensive contact information including grandmother
- Continue to collect information about the mother
- Get developmental information from multiple sources
- Consider ethics of the future
- Consider participant exhaustion
- Obtain funding to maintain staff and as children continue to age
- Plan for the inevitable



Our experience, our protocols has advised other birth cohorts around the world.



For more information



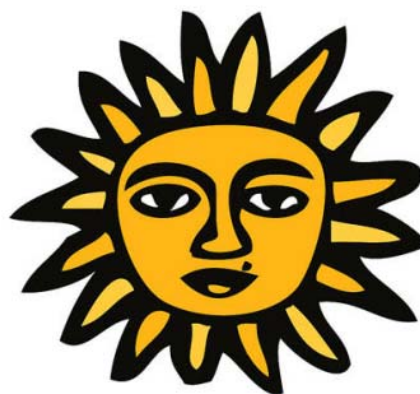
ECHO

<http://www.echochildren.org/>

301-435-2840

CHAMACOS / CERCH

<http://www.cerch.org/>



Thanks to our funders



Thank YOU!!!



www.cerch.org