

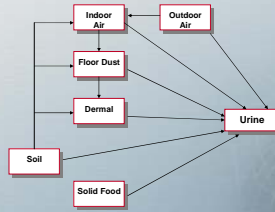
CTEPP Data Considered in SEM and HBM Analyses

- Chlorpyrifos/3,5,6-TCP data for NC and OH children
- Chrysene/1-hydroxypyrene data for OH children

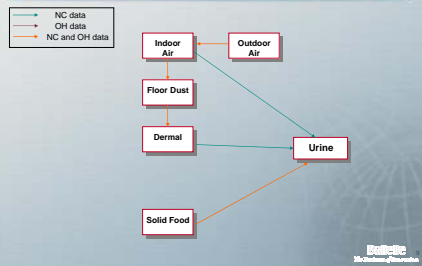
System of linear equations:

- Urine = Outdoor Air + Indoor Air + Floor Dust + Dermal + Soil + Solid Food
- Indoor Air = Outdoor Air + Soil
- Floor Dust = Indoor Air + Soil
- Dermal = Floor Dust + Soil

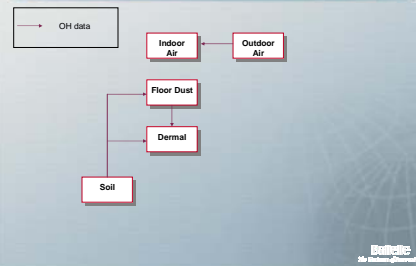
Pathways considered in SEM analysis of CTEPP data



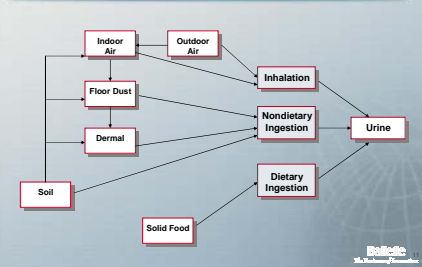
Significant Pathways for Chlorpyrifos/3,5,6-TCP data based on SEM



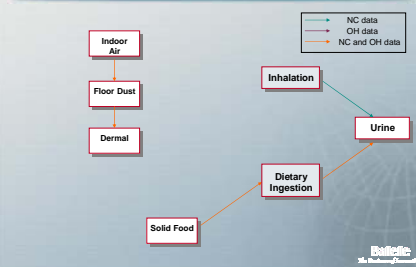
Significant Pathways for Chrysene/1-hydroxypyrene based on SEM



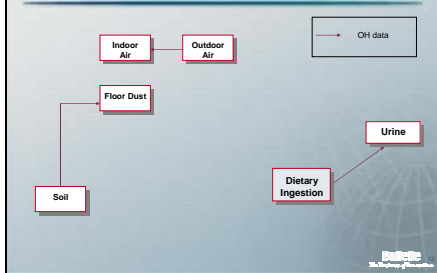
Pathways considered in HBM analysis of CTEPP data



Significant Pathways for Chlorpyrifos/3,5,6-TCP data based on HBM



Significant Pathways for Chrysene/1-hydroxypyrene based on HBM



Recommendations for Future Investigation

- Investigate relationship between potential exposure/dose and frequency of adverse human health effects in children
 - Limited data on adverse health effects attributed to dietary ingestion
- Improve methods and inputs for estimating potential exposure/dose and characterizing exposure routes
 - Include data for locations outside of day care and home environments
 - Improve specifications on absorption fractions
 - Include dermal exposure (more information needed on absorption)
 - More information needed on mouthing tendencies and activity patterns
 - Can indirect ingestion and dermal routes be separated for study?

Recommendations for Future Investigation

- Refine analytical techniques to lower detection limits for pollutants in solid and liquid food
 - Limits ability to characterize dietary ingestion
- Compare dietary exposure/dose measures with values derived from EPA's Dietary Exposure Potential Model
- Measure biomarkers that better characterize exposure to a given chemical in the environment
- Investigate how children's exposure varies over time
 - Time frames under one year (e.g., monthly variation)
 - Are consistent low exposures over extended times important?
- Conduct more small-scale pilot studies

Presentation entitled "Children's Exposure to Pesticides: Studies from Washington State" by Dr. Richard Fenske

Children's Exposure to Pesticides
Studies from Washington State



 **Richard Fenske**
University of Washington
School of Public Health and Community Medicine



Contributors and Support

- » Cynthia Curl
- » Kai Elgethun
- » Kit Galvin
- » Vince Hebert
- » John Kissel
- » Chengsheng Lu
- » Jaya Ramaprasad
- » Jeff Shirai
- » Rene Showlund-Irish
- » Ming Tsai
- » Sarah Weppner
- » Michael Yost
- » NIOSH Agricultural Centers Program
- » EPA STAR Grant Program
- » EPA/NIEHS Center for Child Health Risks Research
- » Dept of Environmental and Occupational Health Sciences

Guiding Principles of the UW Research Program on Children's Pesticide Exposure

- ✓ Identify high risk populations
- ✓ Evaluate exposure to a common class of chemicals
- ✓ Measure multiple exposure pathways
- ✓ Identify opportunities for intervention

Pesticide Exposure Assessment

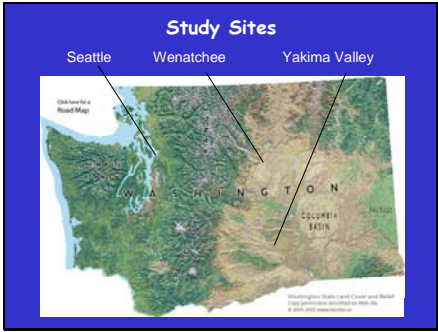
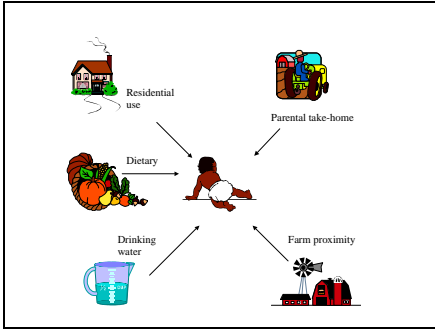
- » **Biological Monitoring Approaches**
 - » Pesticide metabolites in urine
 - » Pesticides in body fluids (blood, saliva)
 - » Biomarkers of effect (e.g., cholinesterase)
- » **Environmental Exposure Assessment**
 - » Measure environmental concentrations
 - » Characterize time-location and personal activities
 - » Exposure and dose modeling

Washington Orchards



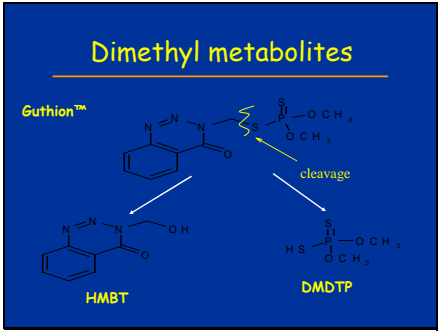
Orchard Pests





Pesticide Use in Washington State Apples

<u>Captan</u>	
<u>Azinphosmethyl</u>	<u>Phosmet</u>
<u>Chlorpyrifos</u>	
<u>Diazinon</u>	
	*
<u>Malathion</u>	
<u>Methyl Parathion</u>	
Mar.	Apr.
May	Jun.
Jul.	Aug.
Sep.	
Fungicide	Insecticide

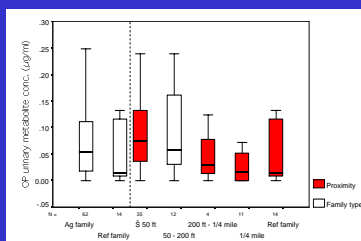


- ### Biological Monitoring Study 1995
- ✓ Children 0-6 years of age
 - ✓ 91 children of agricultural workers
 - ✓ 18 reference children
 - ✓ 2 spot urine samples per child during spraying season

Study Group Definitions

- ✓ **Agricultural Families**
 - One or more household member engaged in pesticide application or field work
- ✓ **Reference Families**
 - No household members engaged in agricultural work
 - Residence >400 m (1/4 mile) from treated farmland

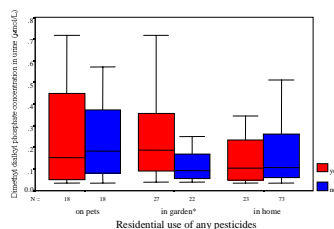
Dimethyl Metabolites ($\mu\text{g}/\text{mL}$) Family Status and Proximity



Seattle Metropolitan Area Study 1998

- ✓ Study population: 50 children from each of two communities
- ✓ Urine sample collection: fall and spring
- ✓ Questionnaire data: residential environment, parental occupation, income level, and pesticide use patterns

Residential OP Use Dimethyl DAP Metabolites

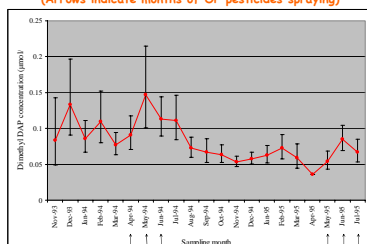


Longitudinal Biomonitoring Study in an Agricultural Community

Koch et al. Environ Health Perspect 110:829-33, 2002

- ✓ Agricultural community in E. Washington state
- ✓ OP pesticide exposure monitored in 44 preschool children for one year
- ✓ Spot urine samples collected on a bi-weekly basis
- ✓ Pesticide spray patterns documented by cooperative extension
- ✓ Para-occupational and proximity factors not significant predictors

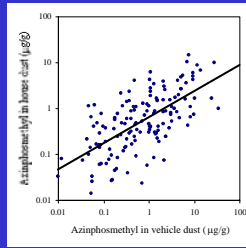
Geometric Means ($\mu\text{mol}/\text{L}$) and 95% C.I. for dimethyl Metabolite Concentrations by Sampling Month (Arrows indicate months of OP pesticides spraying)



Yakima Valley Study of Take Home Pesticide Exposure 1999

- ✓ Children 0-6 years of age
- ✓ 211 children of agricultural workers
- ✓ Vehicle and house dust samples for each agricultural worker
- ✓ Composite urine sample from each child after peak spray season

Azinphosmethyl in House and Vehicle Dust of Agricultural Workers



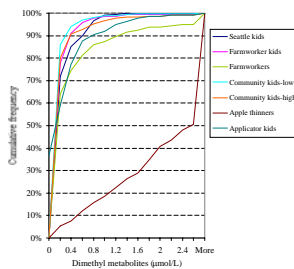
Comparison of WA State Studies



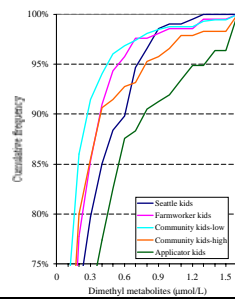
Study Populations

- ✓ Apple thinners
- ✓ Farm workers
- ✓ Farm applicator kids
- ✓ Farm worker kids
- ✓ Kids in an agricultural community
- ✓ Kids in the Seattle metropolitan area

Cumulative frequency distribution of OP pesticide metabolites

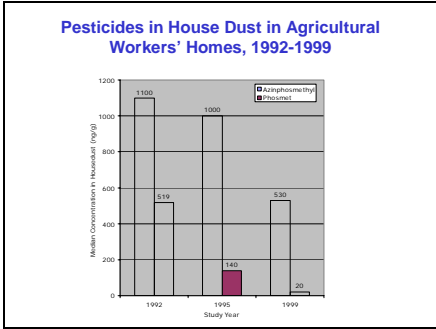


Cumulative frequency distribution- 75th Percentile



Composite Dimethyl Dialkylphosphate Concentrations (nmol/L) for Seattle, Yakima Valley and NHANES-III Children

Population	N	Percentiles	
		50th	90th
Seattle kids	110	117	453
Farmworker kids	211	87	378
NHANES (6-11 yrs)	471	91	460

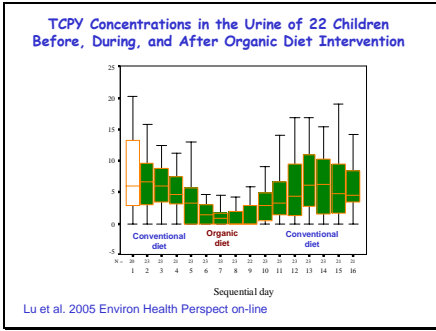


- Conclusions**
-
- ✓ Agricultural workers are more highly exposed than children, regardless of risk factors
 - ✓ Elevated exposures of children in agricultural communities are associated with agricultural spraying
 - ✓ Most children of farm workers and children in agricultural communities have exposures similar to urban children for much of the year
 - ✓ Additional studies should focus on identification of highly exposed sub-populations
 - ✓ Timing of sampling is critical for exposure studies

- Dietary Exposure to OP Pesticides**
Curl et al. Environ Health Perspect 111:377-82 (2003)
-
- Recruitment from two Seattle grocery stores
 - 39 Pre-school children (2-5 yrs old)
 - 3-day diet log kept by parents
 - 24 hour urine sample
 - Children classified by consumption of organic or conventional produce
 - Residential pesticide use minimal

Dialkylphosphate Concentrations in Children's Urine Samples

	Median ($\mu\text{mol/L}$)	
	Dimethyl	Diethyl
Conventional	0.17	0.02
Organic	0.03	0.02



Saliva Biomonitoring A Novel Pesticide Exposure Assessment Approach

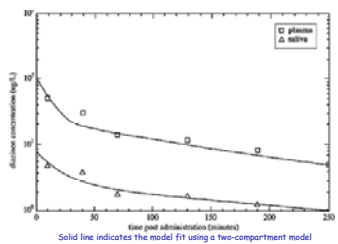
Chensheng (Alex) Lu, Ph.D.
Assistant Professor
Emory University



Feasibility Studies in Animals

- ✓ Intracellular passive diffusion determines appearance of pesticides in saliva
 - Lipid solubility
 - Degree of ionization (pKa)
 - Molecular weight
 - Protein binding
- ✓ Rodent selected as model animal
- ✓ Pesticide administration through i.v. injection, skin or gavage (oral) ingestion
- ✓ Simultaneous arterial blood and saliva collection

Observed and predicted saliva and plasma concentration-time profiles for diazinon in rats after I.V. bolus injection of 1 mg/kg diazinon



Conclusions from Animal Studies

- ✓ Both atrazine and diazinon excreted into saliva,
- ✓ Salivary excretion of atrazine and diazinon unaffected by the dose, route of administration or salivary flow rate,
- ✓ Significant correlation of atrazine and diazinon concentration in saliva and plasma samples
- ✓ Findings suggest that salivary concentrations can be used to predict plasma levels for both pesticides.

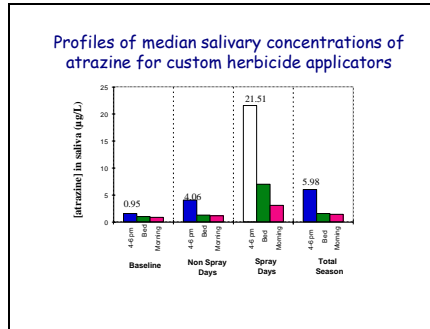
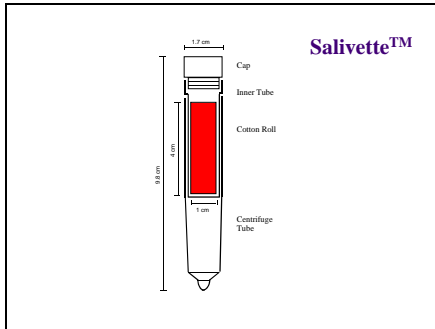
Preliminary Survey of Atrazine Exposure Among Herbicide Applicators

in collaboration with the
National Institute for Occupational Safety and Health
Denovan et al., Environ Health Perspect 73:457-462

- ✓ Evaluate sampling protocol for saliva collection in the field
- ✓ Measure atrazine concentrations in saliva for a cohort of herbicide applicators

Study Design

- ✓ Baseline (3 months prior to application)
- ✓ 15 applicators
- ✓ Sampled every fourth day; 103 events
- ✓ Sampling schedule included post-shift, before bed, and next morning samples
- ✓ Urine, hand wash, skin patches collected by NIOSH



- Conclusions from Field Study**
- ✓ Saliva sampling is practical in the field
 - ✓ Saliva captures the trends of atrazine exposure and elimination in the body
 - ✓ Urine data confirmed the exposure even without atrazine spraying in the field
 - ✓ Lack of plasma samples to confirm the validity of saliva biomonitoring

- On-going Saliva Biomonitoring Studies**
- ✓ Human exposure studies
 - Children's dietary study, Seattle
 - Farm worker family study, Nicaragua
 - Human controlled-exposure study (UC Davis)
 - ✓ Explore other pesticides
 - Chlorpyrifos
 - Permethrin


- Acknowledgments**
- ✓ US EPA STAR Grant R828606
2001 - 2004
 - ✓ US EPA STAR Grant R829364
2002 - 2006
 - ✓ Dr. Dana Barr, CDC Laboratory
National Center for Environmental Health

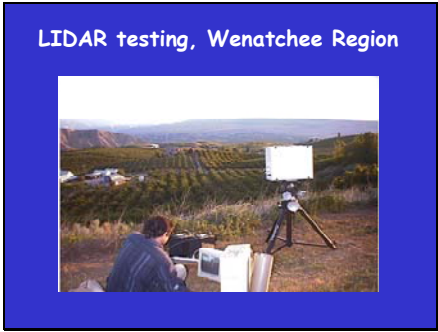


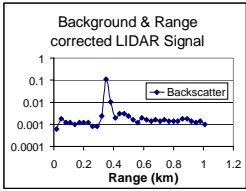


Pesticide Spray Drift Characterization with LIDAR

Michael Yost
 Professor
 Dept of Environmental and
 Occupational Health Sciences
 University of Washington







- Prototype LIDAR has a limited range
- Extending range to 2-4 km requires bigger laser
- Shifting to UV provides stronger signal

Pesticide Spray Drift and Children's Exposure

Kai Elgethun
 Doctoral Candidate
 Dept of Environmental and
 Occupational Health Sciences
 University of Washington



Spray Drift Studies

- » **Spray Drift Modeling Studies**
 - » Human exposure not measured directly
- » **Spray Drift Incident Studies**
 - » Exposure estimated after-the-fact
- » **Washington Aerial Spray Drift Study**
 - » Measure and model spray event
 - » Measure community and residential air and surface levels
 - » Measure and model children's activities and exposures

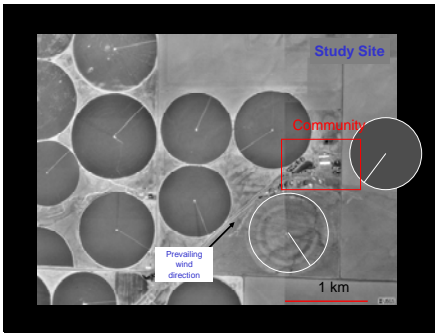
Application Site

- » **Central Washington State**
 - » Dry summer climate
 - » Flat topography
- » **Aerial Applications on Potatoes**
 - » 1-2 times per season every third season
 - » Aerial applications -- fixed wing aircraft



Methamidophos

- » Highly toxic organophosphorus insecticide (Toxicity I)
- » Monitor-4™ 40% emulsifiable concentrate formulation
- » 283 hectares treated @ 1.1 kg a.i. per hectare (1 lb/acre)



Study Site and Population

- » **Agricultural Community**
 - » Surrounded by potato, corn, wheat fields
 - » Single-family residences, recreational facilities
- » **Children**
 - » Parents are farmworkers
 - » Live in community year-round
 - » Ages 3-11
 - » 4 male, 4 female



Informed consent/assent obtained from all parents and children

Estudio de Flujo del Spray de Pesticida

Junta Informativa

Vengan a conocer las investigaciones de la Universidad de la Washington para saber del estudio en su comunidad. Tendrán una comida y bebida.

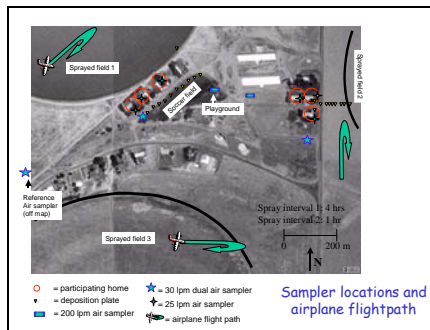
Fecha: 26 de Abril 2002

hora: 6 pm. al. por.

Lugar: Residentes de Washington y al personal de la Universidad de Washington. Todos sus días vividos.

No tienen que ser participantes del estudio. Favor vengán a conocerlos, saber del estudio y disfruten la comida.

Recruitment Poster

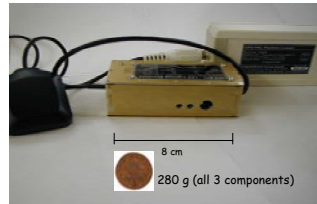


Sampling Procedures

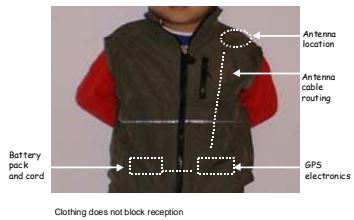
- » **Deposition Samples**
 - » Silica gel chromatography plates
- » **Surface Wipes**
 - » Playground equipment
 - » Toys and apples
 - » Indoor surfaces
- » **Children's Hands**
 - » Isopropanol wipes
- » **Children's Activities**
 - » Global positioning system - personal activity loggers
- » **Air Samples, House dust, Urine samples**



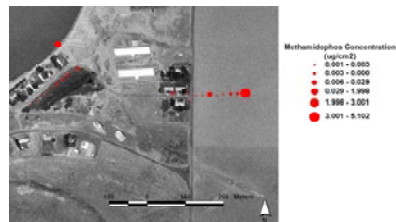
GPS Personal Acquisition Logger (GPS-PAL) (Entertech)



GPS-PALS Unit



Methamidaphos Deposition



Methamidaphos Deposition Morning Spray

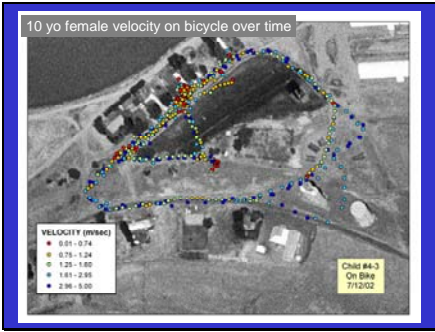
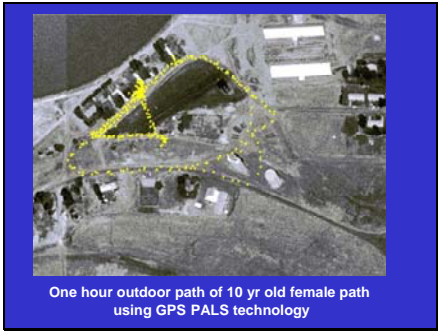
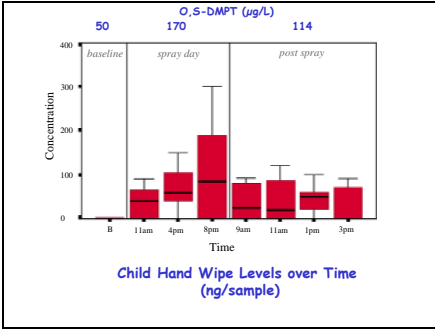
Sampler Location	Loading (ng/cm ²)
North field boundary	2,131
East field boundary	5,653
Soccer field (median)	2.9
East housing (median)	2.4

Methamidaphos on Playground Equipment (ng/cm²)

Sample Source	Morning	Afternoon
Monkey bars - 1	2.09	2.00
Monkey bars - 2	0.57	1.04
Tire swing	0.36	0.98
Baby swing	2.96	5.10

Methamidaphos on Toys, Apples, and Indoor Surfaces (ng/cm²)

Sample Source	Baseline	Post-Spray
Toy - Side yard	nd	0.19
Toy - Back yard	nd	0.37
Toy - Playground	nd	0.14
Apples	nd	nd
Indoor surfaces	nd	nd



- Key Findings**
-
- » **Well controlled aerial application**
 - » Levels at field boundary 1,000X greater than off-target
 - » **Low levels on surfaces in community**
 - » Low ng/cm² on play equipment and outdoor toys
 - » No detectable residues on indoor surfaces
 - » **Children contact with residues**
 - » O,S-DMPT metabolite associated with hand wipe levels and time spent outdoors
 - » **Child activities an important component of exposure analysis**
 - » 8-fold difference between high and low child exposures

- Work in Progress**
-
- » Develop dispersion models for vapors and particles
 - » Estimate dermal contact via deposition modeling and children's activities
 - » Estimate respiratory exposure via air modeling and children's activities
 - » Mass balance analysis of aggregate exposure and biological monitoring
 - » Risk analysis and communication to agricultural community



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**Towards a
Sustainable
Agricultural
Workplace**

Presentation entitled “Assessing insecticide exposures during pregnancy: Results from a biomarker validation study” by Dr. Robin Whyatt

Assessing insecticide exposures during pregnancy: Results from a biomarker validation study




Robin M. Whyatt
Columbia Center for Children's Environmental Health
Funded by: U.S. EPA Star Grant



Three recent epidemiologic studies (EHP, 112,2004) report significant associations between:

- Umbilical cord chlorpyrifos levels and decreased birth weight and length but not head circumference (Whyatt et al.)
- Prenatal maternal urinary TCPY1 levels and decreased head circumference (with PON1 activity as a modifier) but not birth weight or length (Berkowitz et al.)
- Umbilical cord colinesterase levels and gestational age but not maternal urinary TCPY1 levels and birth outcomes (Eskenazi et al.)


13,5,6 trichloro-2 pyridinol



Biomarker Validation Study

102 mother/newborn pairs (2001-04) nested within our ongoing prospective cohort study (N 700 pairs, 1998-present)


Race/Ethnicity: African American and Dominican
Residence: Northern Manhattan and South Bronx
Exclusion: Smokers, Illicit Drug, HIV, Hypertension, Diabetes




Environmental measures of exposure



48 hour personal air 32nd week 2 week integrated indoor air 32nd wk delivery





Biologic Samples

- Repeat maternal prenatal spot urine
- Maternal blood
- Umbilical cord blood
- Postpartum meconium

Background On Meconium

- Meconium accumulates in bowels from 16 weeks gestation.
- Xenobiotics enter meconium through bile excretion and fetal swallowing of amniotic fluid.
- Evidence suggests significant trapping of xenobiotics in meconium.



Insecticides measured

Organophosphates

Chlorpyrifos
Diazinon
Malathion
Methyl parathion

Carbamates

Bendiocarb
Carbaryl
Carbofuran
Propoxur

Pyrethroids

cis-Permethrin
trans Permethrin
Piperonyl butoxide

U.S. EPA phase out of chlorpyrifos/diazinon: 2000-02



Demographics

N=102	
Age	25.2 ± 4.9
Ethnicity	
Hispanic	68%
African American	31%
Marital Status	
Never married	69%
Education	
< High School degree	46%
Annual Household Income	
< \$10,000	43%
Duration of indoor air sampling	7.0 ± 2.3 weeks



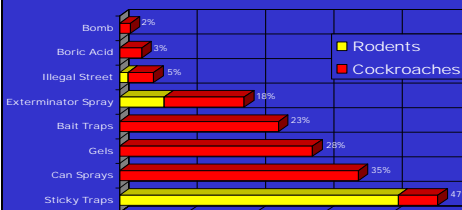
Percent reporting pest sightings and use of pest control between the 32nd week gestation and delivery

N=99

Pest sightings	91%
• Cockroaches	80%
• Rodents	51%
Pest control	61%
• By exterminator	20%



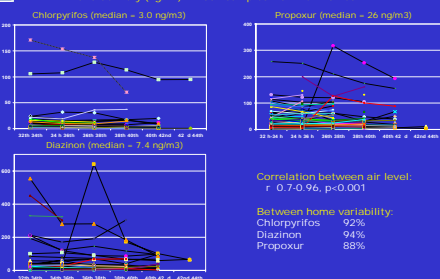
Use of 8 specific pest control methods between the 32nd-34th week of pregnancy and delivery among women reporting pest control use



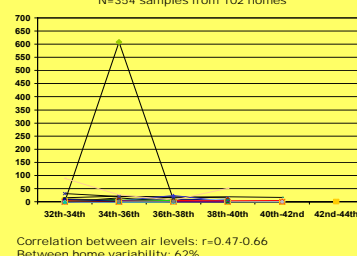
47% used one or more of the higher toxicity methods

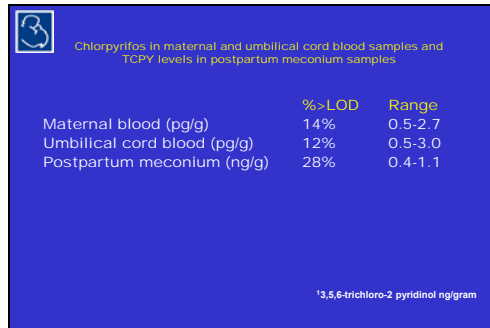
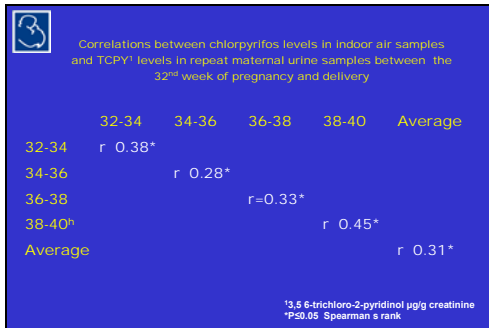
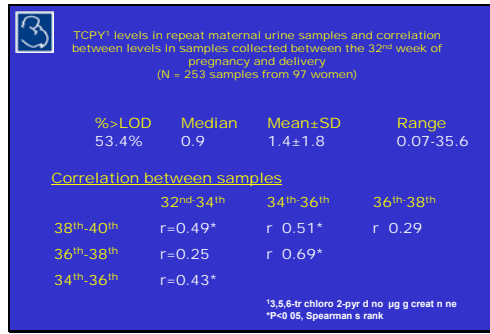
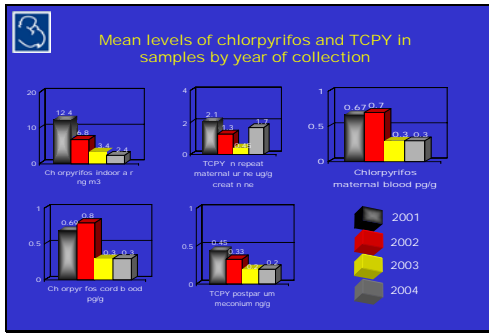
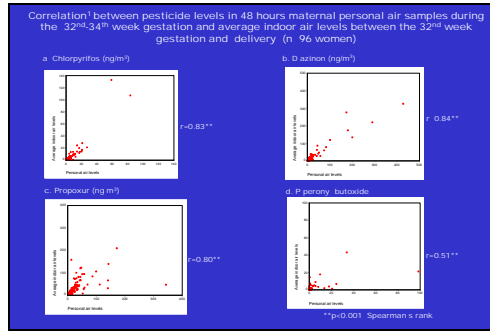
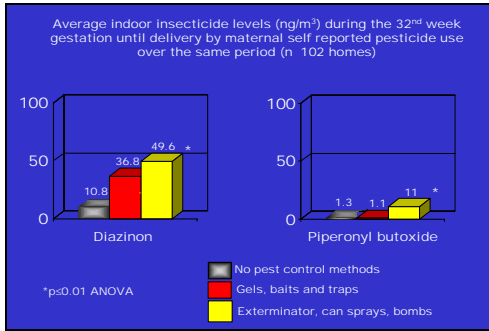


Chlorpyrifos, diazinon and propoxur were detected in 99.7%-100% of indoor air samples collected between the 32nd-34th week of pregnancy and delivery (ng/m³) N= 337 samples from 102 homes



Piperonyl butoxide was detected in 46% of indoor air samples between the 32nd-34th week of pregnancy and delivery (ng/m³) N=354 samples from 102 homes






Correlations¹ between measures of chlorpyrifos in environmental and biologic measures

	Meconium	Maternal blood	Cord blood	Maternal urine
Chlorpyrifos indoor air	r 0.17, p=0.13	r 0.04, p=0.7	r -0.06, p=0.7	r=0.31, p=0.002
TCPY maternal urine	r=0.43, p<0.001	r 0.14, p=0.2	r 0.06, 0.7	
Chlorpyrifos cord blood	r=0.44, p=0.001	r=0.9, p<0.001		
Chlorpyrifos mat. blood	r=0.35, p=0.001			

¹Spearman's rank

- Where do we go from here:
1. Assessment of prenatal exposure to the pyrethroids and other replacement insecticides to chlorpyrifos and diazinon
 2. Additional analyses of prenatal chlorpyrifos and birth outcomes/postnatal development
 - Umbilical cord chlorpyrifos
 - Meconium TCPY
 - Maternal urinary TCPY
 3. Experimental studies
 - Metabolic fate of environmental TCPY/3PBA
 - Relationship between lipid, maternal blood and cord blood insecticide levels with continuous exposure

 Columbia Center for Children's Environmental Health

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Co-Investigators	Research Staff
F.P. Perera	D. Diaz
P.L. Kinney	J. Dietrich
H.F. Andrews	A. Reyes
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D.B. Barr	M. Borjas
G. Rauh	B. Plaza

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Study Participants



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Modeling Children’s Exposure to Pesticides: Issues and Challenges

Halûk Özkaynak
National Exposure Research Laboratory, RTP, NC

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Collaborators

EPA/NERL

- Valerie Zartarian
- Jianping Xue
- Stephen Graham
- Mike Tomero
- James Quackenboss
- Peter Egeghy

EPA/OPP

- Stephen Nako
- David Miller

Allion Science and Technology, Inc

- Graham Glen
- Luther Smith

EOHHS

- Paul Lioy
- Panos Georgopoulos

LBL

- Tom McKone

NCSU

- Chris Frey

Univ. of California, Davis

- Deborah Bennett

Harvard School Of Public Health

- Robert Canales

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Human Exposure Source-to-Dose Modeling Major Components

Contributors

Program Offices
OPP, OPPT, OAQPS
OAR, OSWER, OW

EPA/ORD
NERL
NRMRL
NHEERL
NCEA
NCCT

Universities & Children’s Centers

Other Private & Public Groups

States/Regions

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Exposure Modeling Steps

- Evaluate potential exposure scenarios to single or multiple pesticides (what, where, when, why and by whom)
- Select and apply appropriate aggregate or cumulative exposure/dose model (s) for the scenario (s) of interest
- Evaluate conditions (subjects, locations, sources, pathways) that result in typical and high-end exposures to pesticides of concern
- Determine the intensity, duration, frequency, route and timing of exposures
- Evaluate the health significance of modeled exposures and dose

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Elements of Modeling Analysis

- Identify population groups/ages and microenvironments of concern
- Estimate exposure factors
 - Time-activity data by age, gender, region, etc.
 - Contact/transfer/uptake/PBPK rates or parameters
- Estimate physical factors
 - Source use and emissions
 - Penetration, Infiltration, re-suspension, track-in, volatilization, decay and migration rates
- Application of data and algorithms using a selected modeling structure

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Exposure Model Types

	Mechanistic	Empirical
Deterministic	Mathematical constructs of physical/chemical processes that predict fixed outputs for a fixed set of inputs	Statistical models based on measured input and output values (e.g., regression models that relate air concentrations and blood levels of a chemical or ambient pollutant concentrations with personal exposures)
Stochastic	Mathematical constructs of physical/chemical processes that predict the range and probability density distribution of an exposure model outcome (e.g., predicted distribution of personal exposures within a study population)	Regression-based models, where model variables and coefficients are represented by probability distributions, representing variability and/or uncertainty in the model inputs and parameters.

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and Development (8101R)
Washington, DC 20460

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