Chlorpyrifos: A developmental toxicant

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Chlorpyrifos: #1 Consider the dose
Chlorpyrifos: Impact on the brain

Toxicology:
Massively large literature

Acute exposures result in cholinesterase inhibition and in other toxic pathways.

Biologic activity at lower exposures
  - Upregulation of inflammatory markers
  - Microglia and astrocytes
  - Cytokines IL-6, TNF-alpha
Chlorpyrifos: Adult exposures

Epidemiology:
OP pesticide, developed as nerve gases

Occupational exposures without AChE inhibition:
- Peripheral nerve damage (Starks et al 2012)
- Hearing loss (Crawford et al 2008)
- Physician-diagnosed depression (Beseler et al 2008)
Chlorpyrifos: #2 Consider timing
Chlorpyrifos: Gestational exposures

Motor function
Cognitive deficits
Social skills
Behavioral impairments
ADHD
ASD
...in early/mid childhood

Studies of OP’s

Reviews:
Koureas et al, Toxicol Lett 2012
Munoz-Quezada et al, Neurotoxicol 2013
Gonzalez-Alzaga et al, Toxicol Lettr 2014
U.S. EPA Revised Risk Assessment 2014
High vs. low prenatal chlorpyrifos

Rauh et al, PNAS 2012
Chlorpyrifos: #3 Consider exposure assessment
Chlorpyrifos: Beyond biomarkers

The California Pesticide Use Report

All commercial pesticide applications
Formulation
Crop
Dates
Locations
Chlorpyrifos, PUR, & autism

Shelton et al, Environ Health Persp 2014
Chlorpyrifos: Validation of the PUR

One year comparison of average weekly concentrations of chlorpyrifos detected at three monitoring sites and total reported use of chlorpyrifos per week in an 8 km study area surrounding the monitoring sites.

Wofford et al, Environ Monit Assess 2014
developmental neurotoxicity

#1: low chronic exposure levels
#2: fetal susceptibility
#3: no measurements are perfect
Chlorpyrifos: A developmental neurotoxicant

The evidence is overwhelming at lower doses

Strength
Consistency – multiple domains
Temporality
Robust to measurement methods
Biologic Plausibility – inflammation
Coherence
Thank you!

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End