Pesticides and Health

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What are pesticides?

- insecticides
- herbicides
- rodenticides
- fungicides
- “other living thing”-icides

Pesticide Use

- Hundreds of “active ingredients” forumulated into thousands of products registered for use on food in the U.S. ; formulations include many other ingredients

Source: Goldman 1999

Pesticides are ubiquitous

- 750 million lbs. in agriculture
- 1000 million lbs. in non-agriculture
- 2/3 cities have multiple residues in water
- 2/3 fruits and veggies have residues

Health impacts upstream vs. down stream

- Upstream
  - Manufacture
  - Mixing, loading and application
  - Farm work
  - Pesticide drift
- Downstream
  - Drinking water
  - Food residues
  - Contaminated fish

Attributes of “upstream” health risks

- Acutely toxic materials, e.g., organophosphates
- Materials/applications with higher exposure potential, e.g., pesticide is on foliage or fruit
- Dispersive application techniques, e.g., aircraft spraying, broadcasting
- Broad spectrum agents, e.g. organophosphates
- Chemical vs. biological agents

Attributes of “downstream” health risks

- Persistent materials
- Bioaccumulative substances
- Materials that have high potential to leach into ground water
- Materials that do not break down and/or are difficult to remove from water
- Pesticides that leave residues on foods and/or flow through the food chain (e.g. from corn to animal feed to eggs)

How food pesticides are regulated

- FFDCA: Federal Food Drug and Cosmetics Act
  - 1996 Food Quality Protection Act amendments require a health based standard of a “reasonable certainty of no harm” for allowable residues of pesticides on food. Economics are not considered.
  - Previously there were three standards: risk/benefit for fresh fruits and vegetables and the Delaney Clause (zero risk) for processed foods, giving rise to the “Delaney paradox” (the residue was ‘safe’ on fresh food but not allowed on a process food)
  - Requires EPA to establish “tolerances” – allowable levels of pesticides on foods

How food pesticides are regulated

- FIFRA: Federal Insecticides, Fungicides and Rodenticides Act
- Regulates the use and composition of pesticides (down to an infinite level of detail)
- 1996 Food Quality Protection Act amendments require coordination of registration and tolerance decisions

How pesticides in drinking water are regulated

- FIFRA: Regulates application and SDWA: Safe Drinking Water Act
  - Control of movement to groundwater
  - Control of runoff
- SDWA establishes MCLs (Maximum Contaminant Levels) for pesticides in drinking water
  - Health based standard
  - Feasibility (of removal and/or analysis of the pesticide) is an issue
  - Separate risk assessment strategy (no use of cumulative or aggregate risk, additional 10x factor)

How pesticide “tolerances” are established

- EPA uses Risk Assessment
- Hazard Identification: via test protocols that are required for a food use pesticide (include acute, chronic, cancer, neuro, repro and developmental toxicity)
- Exposure Assessment: utilizes national survey data (HHS/USDA) on the U.S. diet for various age groups, regions, ethnic groups as well as other data

Defining pesticide chronic risks

- Challenges
  - Hundreds of chemistries, thousands of product formulations
  - Relative shortage of human data and need to extrapolate from toxicology studies
  - Many potential exposure scenarios globally

Evaluation of Risk

- Risk assessment
- Risk = hazard X dose
- Four steps in risk assessment have been delineated: hazard identification, dose-response evaluation, exposure assessment, and risk characterization.
- Modifying factors need to be considered as well: age, genetics, nutrition and health status

Hazard issues

- Carcinogenicity
- Neurotoxicity
  - (mostly with in utero exposure)
- Ecotoxicity (best established)
- There are disagreements, largely because of the uncertainties in extrapolating from animals to humans and how difficult it is to do the epidemiology

Toxicity tests (EPA guidelines) required for approval of food use pesticides

- Acute Illness
- Cancer
- Neurotoxicity
- Developmental effects
- Immunologic effects
- Endocrinologic effects
- Reproductive toxicity

Pollutants: Endocrine disruption

- **Endocrine disruption** is defined by the EPA as “an exogenous agent which interferes with the synthesis, secretion, transport, binding action, or elimination of natural hormones in the body which are responsible for homeostasis, reproduction, development, or behavior.”

Potential risks from ED's (1)

- Estrogens:
  - Feminization of male: evidence for increases in hypospadias, undecended testicles and lowered sperm counts
  - Overstimulation of female at times when estrogen is low (in utero, prepubertal, postmenopause): ?polycystic ovary, precocious puberty, premature thelarchy
  - Cancers?: ?prostate, testicle, breast, ovary

Potential risks from ED's (2)

- Antiandrogens
  - Feminization of the male (definitely occurs in laboratory)
  - ?Impacts on the female
- Thyroid
  - CNS development
  - ?Cancer risk

Pesticides suspected as endocrine disruptors

Effect	Suspect pesticides
Estrogenic	aldrin, allethrin, carbaryl, DDT, dicofol, dieldrin, endosulfan, kepone, lindane, methoxychlor, nonachlor, permethrin, toxaphene, triadimefon
Anti-androgenic	Chlordane, DDE (DDT metabolite), iprodione, lindane, linuron, mirex, procymidone, sumithrin and vinclozolin
Thyroid	Acetachlor, alachlor, amitrol, fipronil, heptachlor, malathion, maneb, mancozeb, methomyl, toxaphene, zineb, ziram

http://www.ourstolenfuture.org/Basics/chemlist.htm

Pesticide tolerance assessment science policies

- Definition of “reasonable certainty”
- Assess aggregate risks of exposure to a pesticide across the entire diet as well as from nondiet sources
- Establish tolerances for a “high end” of exposure
- Utilize age specific data to capture diets across the lifespan
- Assess cumulative risks for pesticides with common mechanism
- Additional 10X factor to protect children

Reasonable Certainty of No Harm

- For a carcinogen defined by congress as no more than a 10-6 lifetime risk of excess cancer
- For a noncarcinogen defined by congress as a reference dose (or acceptable daily intake); this involves identification of the “most sensitive” endpoint from studies and application of “uncertainty factors” to determine a “safe” level
- “Risk cup” total allowable amount of a pesticide factors in FQPA 10x factor (see below)

Aggregate exposures

- Diet:
  - Field trials to establish application rates and to assess anticipated residue levels
  - Studies to determine degradation of residues in “post harvest interval” (PHI)
  - Processing studies to determine actual levels in foods
  - Monte Carlo (probabilistic) analysis to determine range of intake for various populations
- Nondiet:
  - Drinking water and residential uses (but not occupational exposures)

What is the “high end” of exposure to food?

Percentile of exposure	Number at a higher level
50 (past practice)	130,000,000
90	26,000,000
95	13,000,000
99	2,600,000
99.9 (current)	260,000

Age Specific Data

- E.g., if the most sensitive endpoint is a birth defect the most relevant exposure distribution would be for women of childbearing age

FQPA 10x Kids Factor

- EPA is required to apply a 10X FQPA safety factor (in addition to the traditional 10X uncertainty factors for interspecies and intraspecies extrapolation) unless there are sufficient toxicity and exposure data to ensure that children will be safe

Cumulative Risks

- Pesticides with a common mechanism of toxicity have to be assessed as a group
- Example:
  - Organophosphates & carbamates

Other factors

- Multiple pesticide exposures may have additive or even synergistic effects
- “Inerts” may comprise more than 90% of the pesticide that is applied. They are often solvents and highly toxic chemicals.

Organophosphates & Carbamates

- Insecticides: 40 OPs in the U.S.
- Inhibit acetyl cholinesterase
- Carbamates share mechanism of action
- Acute and chronic toxicity
- Specific concern re: developmental neurotoxicity
- Food, lawn and household use pesticides (e.g., malathion, chlorpyrifos, aldicarb)

Developmental neurotoxicity of OPs

- Are neurotoxic pesticides especially harmful to developing brains?
- Certain neurotoxic chemicals (PCBs, lead and methylmercury) are 1000 fold more toxic to the developing brain than to adult animals.
- EPA has called in data on developmental neurotoxicity of organophosphate pesticides.
- OPs modulate DNA expression in the developing brain, possibly at levels below those that cause acetyl cholinesterase inhibition

Hazard Data: Where to Find It

- Reregistration of pesticides (1988 law); so called “REDs” are available on line (Reregistration Eligibility Documents)
- Tolerance reassessments (1996 law); EPA must publish a finding showing how it concluded “a reasonable certainty of no harm” (Federal Register)
- EPA FIFRA Science Advisory Panel (www.epa.gov/pesticides)

Pesticide alternatives

- More preferable: less persistent, minimal leaching to groundwater, less dispersive application, minimal exposures to workers, narrow spectrum
- Best: biologicals targeted to specific pests
- Integrated pest management: term is used many ways but at best it means means working within natural systems to control pests
- Organic food production

Thoughts on risk management

- Regional nature of challenges that face farmers (and even global nature of emerging/invasive pests) yet pesticides are managed on a state by state basis
- Need for strong scientific support (e.g. from agriculture schools) independent of the financial interests of pesticide producers
- Emerging markets in biofuels, biopharming, biopolymer production … these products may not be covered under FQPA (if not food)