



ES/RP 531
Fundamentals of Environmental Toxicology

Lecture 1
History; Overview of Concepts

Fall 2005


Instructor


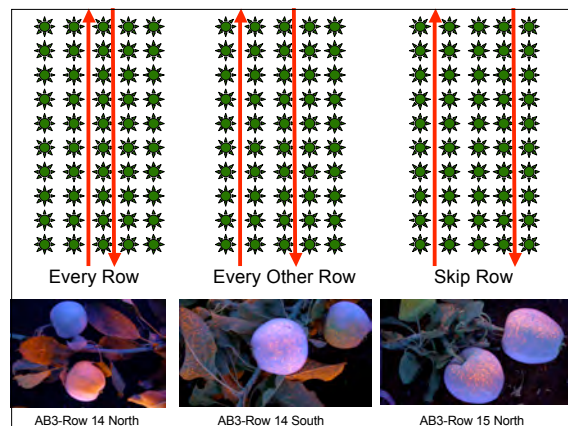
- Allan Felsot
 - Professor, Dept. of Entomology
 - Food & Environmental Quality Lab, WSU-TC
 - afelsot@tricity.wsu.edu (best way to communicate)
 - 509-372-7365
 - URL <http://feql.wsu.edu>
 - 30 years studying environmental chemistry & toxicology
 - Soils & water issues
 - Insect toxicology
 - Remediation of pesticide waste
 - Exposure Assessment
 - Agricultural Biotechnology

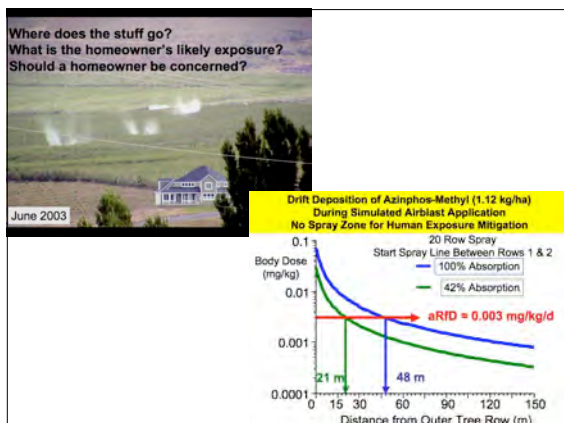
Current Research Interests

Sprayer Technology Project

- Research projects funded by the WA Tree Fruit & Research Commission & US EPA Region 10
 - Spray drift research for enhancing IPM & environmental stewardship
 - Use of alternative sprayer technology & practices to reduce application rates, worker exposure, and drift
 - Development of buffer zones at the ag/urban interface, protection of water quality, and validation of AgDrift model for orchards





ES/RP 531 -- Course Content

- Will study fundamentals of environmental toxicology in the context of the risk assessment paradigm
 - Hazard ID
 - Dose-Response
 - Exposure Assessment
 - Risk Characterization

Course Content

- For example, we will examine the endocrine disrupter hypotheses and potential effects at higher levels of organization, but the discussion will be considered as hazard identification within the context of risk assessment
- We will examine how interactions of chemicals with environment influences bioavailability and exposure, but the discussion will be considered as exposure assessment within the context of risk assessment

Course Content

- Focus will be on basic concepts, using specific invertebrate and vertebrate models (will avoid rat toxicology wherever possible)
- Focus will not be chemical specific, but will use specific chemicals to illustrate fundamental knowledge of toxicological hazards

FYI: ES/RP 532; Applied Environmental Toxicology

- Offered every other year in alternation with ESRP 531 (Next class: Fall 2006)
- Focus on specific groups of contaminants examining issues from A to Z
 - Manufacture & Release
 - Physicochemical Properties
 - Environmental Chemistry
 - Toxicology (mammalian & environmental)
 - Epidemiology

Textbook???

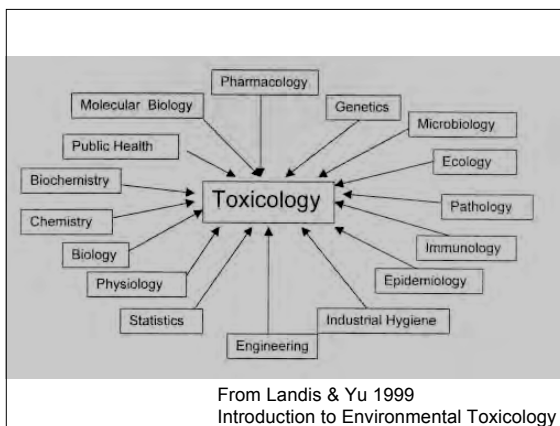
- My philosophy is that the field is too dynamic, too interdisciplinary, and too broad (i.e., many perspectives) to capture in one text
- Therefore, I gather the information and make it available to you in the form of detailed lecture notes and PowerPoint presentations to highlight important points
- All lectures posted on the WSU FEQL website, URL <http://feql.wsu.edu>
 - Link to the teaching page; link to ES/RP 531
- Send me your email addresses & I will email you the materials, especially the papers that I want you to read
 - Owing to copyright restrictions, I will not post published papers

Evaluation

- Four take-home evaluations, each worth 25% of grade
- The evaluations are open-book; I don't care what resources you use!!!!
- Short answer and cogent narrative essays
 - "Story" problems & critical analysis of papers
- Complete the test digitally and email me your answer by 5 pm of the following class date

Toxicology

- "Science of poisons"
 - Too simplistic
- Evolved from a diversity of fields and encompasses a diversity of academic disciplines today (multidisciplinary)
 - Common thread
 - Chemicals, exposure, adverse effects
- Goal:
 - Prediction of human/environmental health effects



Toxicology

- "...a study of the interaction between chemicals and biological systems in order to quantitatively determine the potential for chemical(s) to produce injury which results in adverse effects in living organisms, and to investigate the nature, incidence, mechanism of production, factors influencing their development, and reversibility of such effects." (Ballantyne et al. 1999)

Expansion of Toxicology

- Exponential increase in the number of synthetically produced industrial chemicals
- Major increase in the number and nature of new drugs, pharmaceutical preparations, tissue-implantable materials, & devices
- Increase in number & types of pesticides and other substances used in ag & food industry
- Mandatory testing and regulation
- Enhanced public awareness of potential effects
- Litigation

Key Issues in Toxicology

- Potential to cause injury predicated on close contact with tissue or organism
- Observed toxicity related quantitatively to degree of exposure
 - Dose-response relationships are of prime importance in confirming causal relationship between exposure and effect
 - Dose-response relationship important for assessing relevance of observed toxicity to practical exposure conditions
 - Dose-response relationships allow hazard evaluations & risk assessment

Toxicology = Many Subspecialties of Study

- Clinical
- Veterinary
- Forensic
- Occupational
- Pharmacological
- Toxinology
- Regulatory
- Laboratory
- Environmental

Environmental Toxicology

- Assesses the effects of contaminants, usually at low concentrations, released from commercial and domestic sites into the immediate environment and subsequently distributed widely by and in air, water, soil, and biota
 - Uses disciplines of study common among all toxicology subspecialties

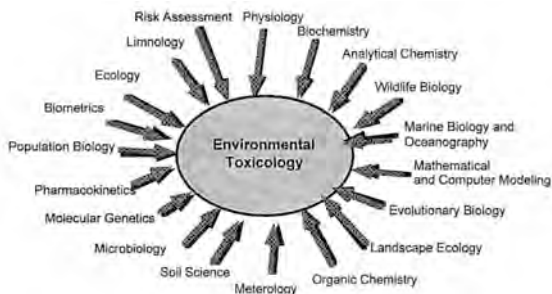
Environmental Toxicology vs. Toxicology

- Toxicology is usually mammalian oriented with extrapolations to humans, whereas environmental toxicology is focused on environmental effects
 - Environmental effects encompasses all biota in all environments
- Toxicology concerned with effects on individual
 - Environmental toxicology has an objective of focusing on increasing higher levels of organization
 - Individual-->Population-->Community-->Ecosystem

Toxicological Tools

- Chemistry (analytical, organic, bio)
 - Biochemical toxicology
 - Pharmacokinetics/pharmacodynamics
 - Molecular/Cellular reactions
 - Mode of Action
- Ecology
 - Ecotoxicology
 - Effects at higher levels of organization

Toxicological Tools



From Landis & Yu 1999
Introduction to Environmental Toxicology

Historical Roots

- Prehistoric culture familiar with toxic effects of animal venoms and poisonous plants
- Ebers papyrus (1500 BC)
 - Egyptian document with recipes containing recognized poisons
- Greek/Roman Culture
 - Many references to poisonous plants and antidotes

Historical Roots

- Middle Ages
 - Poisoning as a political weapon
 - Rudiments of experimental toxicology practiced by Catherine de Medici in France
 - Use direct poor and sick as guinea pigs to derive the most effective poisons
 - Noted rapidity of response ("onset of action")
 - Noted the effectiveness of a compound ("potency")
 - Noted the degree of response in specific body parts ("specificity"; "site of action")
 - Noted the complaints of the victim ("clinical signs & symptoms")

Historical Roots

- Paracelsus (1494 - 1541); recognized creator of scientific discipline of toxicology; three important concepts:
 - The toxicon or toxic agent is a chemical entity
 - Modern QSAR studies
 - Response to a substance is related to dose
 - Experimentation essential
 - Distinguish between therapeutic and toxic properties
 - Distinguishable only by dose
 - Specificity of chemicals and therapeutic or toxic effects
 - Toxicology covers a wide area
 - Paracelsus interest extended from detection or accidental or intentional poisonings through environmental factors affecting populations and occupational diseases

Historical Roots

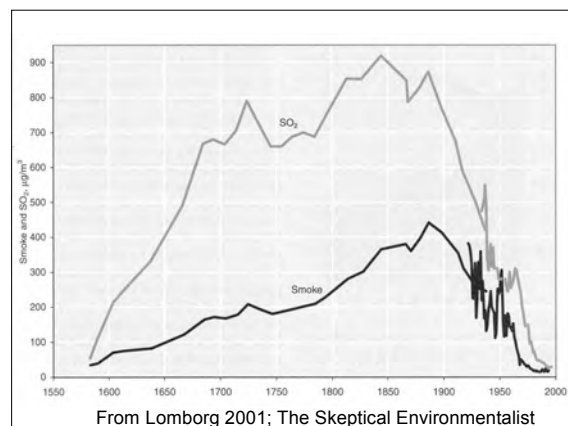
- Matteiu Joseph Bonaventura Orfila (1787 - 1853); father of modern toxicology
 - First systematic correlation between chemical and biological information of known poisons
 - Studied effects in thousands of dogs
 - Viewed toxicology as a distinct discipline
 - "Traite Des Poisons, ou Toxicologie Generale"
 - Pointed to the necessity of chemical analysis for legal proof of lethal intoxication and devised methods for detection of poisons
 - Developed the analytical approach that has become the basis of forensic toxicology

Historical Roots

- Claude Bernard (1813 - 1878)
 - Studied mechanisms of action of curare (one of several arrow poisons used by natives)
 - Recognized that "the physiological analysis of organic systems...can be done with the aid of toxic agents"

Roots of Environmental Tox.

- Concerns about polluted environment date back to Roman times and hundreds of years to concerns over "foul" water and air in England
- Indeed, not until modern times, was air of England "cleaned up"



Roots of Environmental Tox.

- Paul Muller discovers insecticidal properties of DDT
 - Wins Nobel prize in 1949
 - Used extensively during WWII
 - Domestic use grew rapidly by 1950
 - Registration suspended in US in 1973
 - Probably more research on this xenobiotic than any other

Roots of Environmental Tox.

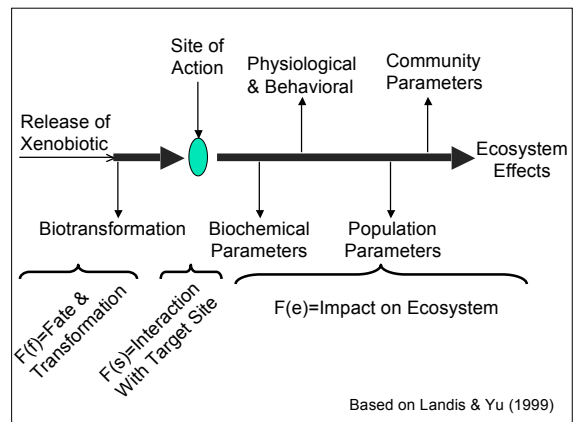
- Rachel Carson's Silent Spring (1962) commonly (mythologically) considered as progenitor of environmental awareness with regard to toxics
 - Challenge: pick up a copy of Silent Spring and check the references
 - By the late 1940's and into the 1950's, numerous papers were published on what would now be considered environmental toxicology of DDT

Roots of Environmental Tox.

- The origination of environmental toxicology may have actually started even before the era of DDT
 - Insect toxicologists needed to know how compounds worked in the environment to control insects
 - Examination of the Journal of Economic Entomology shows major environmental toxicology themes prior to Carson's book
 - Measurement of toxicity; symptomology, mode of action, metabolism; insecticide resistance; pesticide selectivity & comparative toxicology; insecticide residues & analytical methods; hazard evaluation; environmental chemodynamics

Sensitivity of Entomologists

- Sheppard, 1939
- Wrote book on "The Chemistry & Toxicology of Insecticides"
 - "Chemical control as the advantage that it brings prompts relief from the depredations of insects. On the other hand it is frequently only a palliative and should be accompanied by steps taken to eliminate the sources of infestation. The relation of permanent measures to the economy of other forms of natural life, however, needs full consideration. This was shown recently in the conflicting methods required for mosquito control and for wild game conservation."



Linear vs. Non-linear Thinking

- The hierarchy of events depicted by the three functions seems linear
 - i.e., it implies that there is some stable equilibrium state of the ecosystem that will return when the toxicant stressor is removed
 - If this were true, then remediation of any system would seek return of this state
- In reality, however, the ecosystem is chaotic (which means the system exhibits nonlinear dynamics), and once perturbed (naturally or synthetically) it will not return to some idealistic equilibrium state

Non-Linear Dynamics & the Community Conditioning Hypothesis

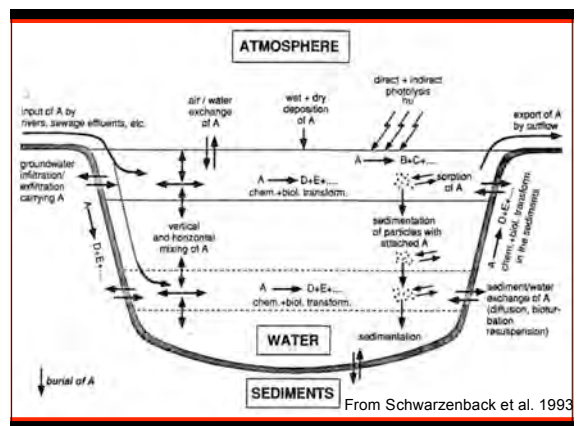
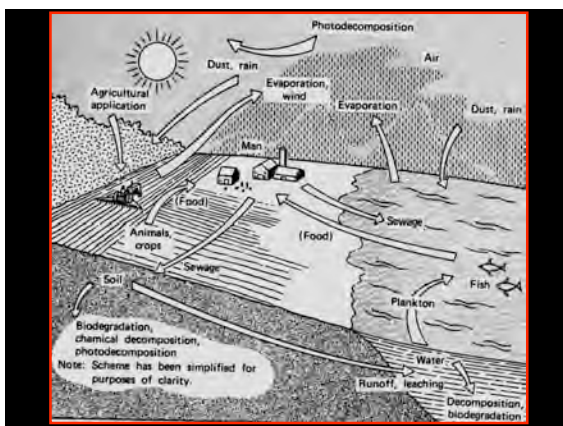
- Landis et al. have argued that the ecosystem itself, which is nonorganismal, retains a historical "memory" that interacts (gives feedback) to the organisms themselves
 - They have shown in artificial laboratory housed ecosystems (microcosms) that effects persist long after a toxicant has dissipated below known levels, suggesting that the ecosystem retains information about events that have happened within itself
 - For example, if resistant individuals gained prominence, this change in gene frequency (a biotic character) would be retained as part of the ecosystem over a long period and cause changes in the relationships between organisms
- Must account for this complicated feedback system when making decisions about remediation

Are We Stuck with What We Can Measure

- Despite the attractiveness of the community conditioning hypothesis, we still have to deal with the three functions that can possibly lead to effects at higher levels of organization
- At least we can strive to make predictions about individuals and perhaps populations

Fortunately, We Have a Theoretical Framework

- With a theoretical framework to aid understanding the "functions" controlling toxicant-organism interactions, we can still make predictions about the likelihood of adverse effects
 - Environmental Chemodynamics
 - Pharmacodynamics/Pharmacokinetics
 - Also called toxicodynamics/toxicokinetics



Environmental Chemodynamics

- Goal: prediction of adverse effects
- Objective: understand distribution of chemicals in environment that lead to potential exposure
- Holistic and based in physical chemistry
 - All is controlled by thermodynamics and kinetics
- All environmental compartments interface with one another

Environmental Chemodynamics Focus Areas

- Physicochemical properties
- Partitioning
- Attenuation
- Transport
- Modelling

Toxicodynamics/Toxicokinetics

- Absorption rate/amount
- Distribution in the body
- Metabolism
- Excretion
- Target site interactions

