Exposure to Toxic Chemicals in Your Everyday Environment

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Western Michigan University
Modern Life: Human Made Chemicals in the Environment

• Pesticides and fertilizers used in agriculture
• Industrial chemicals
• Daily use chemicals (home, work)
• Global transport due to the weather patterns (major contamination in the arctic)
• Human made chemicals are everywhere on earth
Favorite Ide Frog Studies

• Related to the Environment
  – The herbicide, atrazine, alters metabolic gene expression that burns up tadpole fat and muscle, decreasing growth and increasing mortality by metamorphosis
  – PCBs, industrial contaminants found in Great Lakes watersheds (e.g., Kalamazoo River) and worldwide, alters developmental tadpole gene expression including that of endocrine genes needed for on-time metamorphosis
  – Methylmercury, a contaminant from coal fired power plants, reduces cytokine protein expression during development of the tadpole nervous system resulting in abnormal motor behavior
Atrazine Effects on Growth, Metabolism, Functional Gene Expression, and Mitochondrial Disposition in Frogs

• Atrazine Effects on developing frogs includes dramatic changes in metabolic gene expression (Dr. Anna Langerveld; Ph.D. to Ron Celestine).

• Fat metabolism is altered, leaving protein metabolism to take up the slack; mitochondria that produce the cell’s energy are degenerating (Renee Zaya, Ph.D. candidate).
Atrazine Alters Fat Deposition in Developing Frogs

• Fat bodies are used by frogs after metamorphosis for reproduction
• Atrazine dramatically reduces fat body size

Control (0 ppb) female stage 62 tadpole fat body. Bar =1mm

Exposed (400 ppb) female stage 62 tadpole fat body. Bar =1mm
Normal Male and Female Gonads in Xenopus Frogs (from Hayes et al)
Atrazine Induced Hermaphroditic Gonad in a Xenopus Frog (from Hayes et al)
Parkinson's Disease

• Currently scientists have little understanding of what causes Parkinson's, where a tiny group of dopamine-producing neurons deep within an area of the brain known as the substantia nigra die.

• This cell death leads to a shortage of the neurotransmitter dopamine and to the tremors, rigidity, and slow movement that mark the disease as it progresses slowly over a period of years or decades.

• Parkinson's affects about 1 million people in North America.
α-synuclein Aggregates Are Associated with Parkinsonism

- A. Normal section from postmortem human brain (ponto-cerebellar tract in pons) showing light background ICC staining for α-synuclein.
- B. α-synuclein aggregates as glial cytoplasmic inclusions appear in a similar section from an MSA patient with Parkinsonism.
Pesticides and impairment of mitochondrial function in relation with Parkinsonian syndrome.


- The Parkinsonian syndrome induced by pesticides is associated with the impairment of mitochondrial function.
- Toxicants that inhibit selectively NADH-dehydrogenase activity, as rotenone or pyridaben, also show a selective inhibition of O2 uptake in rat brain.
- Paraquat produced a non-selective inhibition affecting all the respiratory chain complexes.
Gene Expression Deficits in Brain Tissues from Patients with Parkinsonism Resemble Those from Pesticide Exposed Animals

Gene Expression Changes in Postmortem Tissue from the Rostral Pons of Multiple System Atrophy Patients

Anna Jelaso Langerveld,1 Daniel Mihalko,2 Cari DeLong,1 Jeff Walburn,1,3 and Charles F. Ide1,3*
Study of the nongenetic causes of Parkinson's disease (PD) was encouraged by discovery of a cluster of parkinsonism produced by neurotoxic pyridine 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in the 1980s. Pesticide exposure has been associated with increased risk in many studies. Other proposed risks include rural residence and certain occupations. Cigarette smoking, use of coffee/caffeine, and non-steroidal anti-inflammatory drugs (NSAIDs) all appear to lower risk of PD. Dietary lipid and milk consumption, high caloric intake, and head trauma may increase risk. The cause of PD is likely multifactorial. Underlying genetic susceptibility and combinations of risk and protective factors likely all contribute. The combined research effort by epidemiologists, geneticists, and basic scientists will be needed to clarify the cause(s) of PD.
Big Picture

• Aging – caused by inefficient mitochondrial electron transport; free Oxygen radicals damage DNA, proteins, etc.
• Proteasome stops removing worn-out, misshapen proteins, which leads to more cellular inefficiency, and ultimately cell death
• Pesticides cause brain cells to age prematurely by disrupting electron transport and proteasomal function
• Thus, environmentally induced neurological disease should increase as more pesticides are placed in the environment
• More Parkinsonism cases occur in geographic areas where pesticides are heavily used (e.g., the Midwest)
Industrial Contaminants

• Polychlorinated biphenyls
• Mercury
209 Different Congeners of PCBs

- **Co-planar**
  - Most toxic
  - Need to be in co-planar or flat position to bind to receptors

- **Non co-planar**
  - Responsible for disrupting calcium homeostasis, neurological and neuromuscular function
Kalamazoo River Watershed – Part of the Lake Michigan Basin
Favorite Ide Lab Frog Studies

– PCBs, industrial contaminants found in Great Lakes watersheds (e.g., Kalamazoo River) and worldwide, alters developmental tadpole gene expression including that of endocrine genes needed for on-time metamorphosis
Morphology and Behavioral Effects Associated with Exposure to Aroclor 1254

- Decreased/aberrant escape swimming behavior
- Paralysis
- Parkinson’s-like, uncontrolled twitching
- Shorter, crinkled tails
Aroclor 1254 Alters Melanocyte Structure

- Change in melanocyte shape
- PCB exposure blocks melanocyte arborization in response to light
- UV light from the sun can now mutate brain cell DNA
Stage 46 Xenopus tadpole
Gene Expression in 18 Day Old Tadpoles: Bioindicators of Exposure

- Exposure to low levels of Aroclor 1254 (5 and 50 ppb) increased gene expression
  - NGF
  - β-actin
  - CPP32β
  - ICE
  - POMC
  - p53
Decreases in Gene Expression Are Predictive Bioindicators

- Decreased gene expression at high doses (700 ppb) correlated with decreased survival and the onset of adverse health effects:
  - NGF
  - β-actin
- Decreases in gene expression occurred in tadpoles exposed to 300 ppb and greater
PCBs Alter Hearing Development in Frogs (and Humans)

Eating Fish
Introduction

- Contaminants attach to sediment, which is eaten by zooplankton then bioaccumulated, then biomagnified from smaller to larger fish.
- Concentration of chemicals can be millions of times higher in top predators than in water.
- May take years of eating contaminated fish to cause adverse health effects.
- Fish containing harmful chemicals may not look, smell or taste bad.

<table>
<thead>
<tr>
<th>Great Lakes</th>
<th>PCBs</th>
<th>Dioxins</th>
<th>Mercury</th>
<th>Chlordane</th>
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<tbody>
<tr>
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<tr>
<td>Lake Ontario</td>
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</table>
Fetal Exposure to PCBs

• Fetus is more sensitive
  – Crosses the placenta
  – Accumulates in breast milk
  – Some studies show
    • Lower birth weight
    • Smaller head
    • Premature birth
    • Lower IQ
“Effects of PCB exposure on Neuropsychological Function in Children”

• PCB adversely effects neurodevelopment
  – Taiwan
  – Michigan
  – New York
  – The Netherlands
  – Germany
  – The Faroe Islands
# Sport Fish Advisory Example

**Illinois Lake Michigan Fish Advisory**

**Cook and Lake Counties (Illinois)**

**Species and Meal Frequency**

<table>
<thead>
<tr>
<th>Fish</th>
<th>Frequency</th>
<th>Size Limit</th>
<th>Contaminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinook Salmon</td>
<td>All Waters</td>
<td>Less than 32&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>All Sizes</td>
<td>1 meal/month</td>
<td></td>
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<tr>
<td></td>
<td>- or -</td>
<td>Larger than 32&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>6 meals/year</td>
<td></td>
<td></td>
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<tr>
<td>Coho Salmon</td>
<td>All Waters</td>
<td>Less than 22&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>All Sizes</td>
<td>1 meal/week</td>
<td></td>
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<tr>
<td></td>
<td>- or -</td>
<td>Larger than 22&quot;</td>
<td>PCBs</td>
</tr>
<tr>
<td></td>
<td>1 meal/month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rainbow Trout</td>
<td>All Waters</td>
<td>Less than 22&quot;</td>
<td>PCBs</td>
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<td>All Sizes</td>
<td>1 meal/month</td>
<td></td>
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<td></td>
<td>- or -</td>
<td>Larger than 22&quot;</td>
<td>PCBs</td>
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<tr>
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<td>6 meals/year</td>
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<td>Brown Trout</td>
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<td>1 meal/month</td>
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<tr>
<td></td>
<td>- or -</td>
<td>Larger than 22&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>6 meals/year</td>
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<td></td>
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<td>Channel Catfish</td>
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<td>23&quot; to 27&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td></td>
<td>6 meals/year</td>
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<tr>
<td>Lake Trout</td>
<td>All Waters</td>
<td>Less than 27&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>All Sizes</td>
<td>1 meal/month</td>
<td></td>
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<tr>
<td></td>
<td>- or -</td>
<td>Larger than 27&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td></td>
<td>Do Not Eat</td>
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<td>Yellow Perch</td>
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<td>Less than 22&quot;</td>
<td>PCBs</td>
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<td></td>
<td>All Sizes</td>
<td>1 meal/week</td>
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<tr>
<td></td>
<td>- or -</td>
<td>Larger than 22&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>1 meal/month</td>
<td></td>
<td></td>
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<td>Carp</td>
<td>All Waters</td>
<td>Less than 22&quot;</td>
<td>PCBs</td>
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<tr>
<td></td>
<td>All Sizes</td>
<td>1 meal/month</td>
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<tr>
<td></td>
<td>6 meals/year</td>
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</table>

*Figure 1-2. Illinois Lake Michigan Fish Advisory*

*Source: [www.idph.state.il.us/envhealth/factsheets/fishadv.htm](http://www.idph.state.il.us/envhealth/factsheets/fishadv.htm)*
Mercury

• 205,583 lake acres (all inland lakes) in Michigan, 478 river miles under fish consumption advisory
• Mercury can’t be removed from fish because it is contained in meat, not fat
• No more than a meal a week of contaminated fish
• Fish low in mercury include shrimp, canned light tuna, salmon Pollock and catfish. Fast food and fish sticks are usually low as well
Even More Immediate Toxicants

• Ethyl Alcohol (wine, beer, gin, vodka, scotch, etc.)
• Chemicals in Cosmetics (acetone, isopropyl alcohol, hydroquinone, botox)
Fetal Alcohol Syndrome: Tadpole Model

- Ethanol disrupts connexin 43 expressing cells in the rhombomeres of *Xenopus laevis* (Bharti Katbamna, Tracy Barsheff, Charles F. Ide)
Chemicals in the Home and Workplace: Acetone

• Solvent used in nail polish remover, paint remover, glue, cleaners, tobacco smoke

• Sub-chronic exposure (inhalation 10% of your time) causes central nervous system depression, irritation of eyes, nose, throat; neurobehavioral changes
Chemicals in the Home and Workplace: Isopropyl Alcohol

• Becomes acetone in your body
• Inhalation causes irritation of eyes, nose, and throat, central nervous system depression
• Skin exposure causes eczema, sensitivity, and for high exposures (sponge bath to lower fever), respiratory distress, stupor, and coma in children
• Released from cosmetics, liniments, skin lotions, permanent wave lotions, pharmaceuticals, hair tonics, skin astringents, mouth washes, perfumes, oils
Chemicals in the Home and Workplace: Hydroquinone

• Used in photographic development, skin lighteners, hair dyes, other cosmetics, cigarette smoke
• Skin application can produce ochronosis (adverse pigmentation, calcification and cartilage inflammation); also, irritation, staining, and allergic contact dermatitis
• Airborne exposure with other toxicants can produce corneal ulcers, opacity, loss of vision several years after exposure
• Highly toxic to organisms in the environment
Chemicals in the Home and Workplace: Botox

- Toxin produced by Clostridium botulinum bacteria (most toxic substance known to humans; found in improperly preserved food)
- Blocks neuromuscular transmission (causes paralysis); injected to temporarily remove frown lines and brow furrows
- Adverse events from cosmetic use includes headaches, focal facial paralysis, muscle weakness, dysphagia, flu-like syndromes, and allergic reactions
- In cosmetic use, clients sometimes complain of inappropriate facial expression such as drooping eyelid, uneven smile, loss of ability to close the eye for up to 6 weeks.
Conclusion I

• Our modern lifestyle is challenging our genes, cells, and tissues to deal with a variety of stressors, some of which we have not had to solve during our long evolution.

• People are exposed daily to more and more chemicals that are now the basis of our industrial and agricultural productivity, and, in some cases, our personal grooming.

• In the short term, these chemical exposures can be irritating and cause minor health problems; in other cases, chronic exposure can produce cancer, neurological disease, and immune system dysfunction.
Conclusion II

• Human genome analysis is revealing more everyday about how good and bad health are caused by our hidden genetics responding to environmental (chemical) exposures

• Most of us do not know our specific genetics, what we are susceptible to, and what we can solve/resist

• So avoid the chemicals! Be careful!