"I need Help, My dad Just drank some poison ..." 911 Call
EPIDEMIOLOGY

• In 2007, 95,657 pesticides exposures were reported to the NPDS of the American Association of Poison Control Centers (AAPCC).

• 43,469 of those were Children under the age of 6 years old.

• 16 Deaths registered.
The study found the highest levels of pesticide residue in peaches, apples, pears...

...and spinach.
Some unique Characteristics...

- Remarkable amount of Compounds.
- Complex Clinical Syndromes.
- Management usually requires using Poison Index or Calling Poison Control.
- Pesticides have Class-specific Toxicities.
- Local and Systemic effects.
- Most need supportive care.
- Some have specific antidotes that could be lifesaving measures.
WARNING:
Pesticides are Dangerous to Your Health!

Stop Endocrine Disrupting Chemicals!
I. INSECTICIDES

Divided in 5 Major Groups / Classes:

1. Organic Phosphorus Compounds
2. Carbamates
3. Organochlorines
4. Pyrethrinines
5. DEET

In 2007:
- 49,564 Exposures
- 19,757 to children <6 years old
- 10 Fatalities
- 198 cases of Major toxicity
- 32 of them Organophosphorus compounds
Special Considerations - ONE

- Organic Phosphorus Compounds (OPC) and Carbamates are the 2 groups of Cholinesterase-inhibiting pesticides that produce MOST of the human toxicity.
- Both rise the concentration of Acetylcholine (Ach) at Muscarinic and Nicotinic receptors.
- Lead to the Syndrome of Cholinergic excess.
- Most lethal insecticides used in America.
- Among the MOST LETHAL poisonings.
Foolish Frogs
Special Considerations - TWO

- Fatality rates as high as 23%.
- Direct dermal contact may be rapidly poisonous
- Commonly used for Homicides.
- First agent Synthetized in 1854, and “Tasted” by Clemont (TEPP) Tetra Ethyl Pyrophosphate
- More than 50,000 agents Synthetized
Questions to be ASKED !!!

- First Aids implemented PTA
- Prehospital Interventions
- Decontamination
- Product name
- Manufacturer
- Concentration and Formulation
- Circumstances of Exposure
- Amount
- Onset of Symptoms
- Patient’s Age and Medical History
- Other Co ingestions / Medications
"As we had hoped, it kills weevils instantly. It also kills blue birds, snow geese, ground hogs, manatees, butterflies, swordfish and Alaska king crabs. Will that be a problem?"
Ia. – OPC

• Inhibition of Ach leads to the accumulation in the NMJ and over stimulation of the Ach Receptors

• OPC bind IRREVERSIBLY to the Cholinesterase, inactivating the Enzyme completely

• AGING (24 – 72 hrs)

• Once it occurs, the Enzymatic activity of Cholinesterase is PERMANENTLY DESTROYED – takes weeks for new synthesis.

• Treatment has to be Given prior to AGING.
Most Common OPC

- Malathion
- Parathion
- Chlorpyrifos
- Diazinon
- Orthene

- They have been use as chemical Warfare agents since WWII: Sarin, Tabun, VX, Soman.
OPC – Clinical Features

- Variety of CNS manifestations, Muscarinic, Nicotinic and Somatic Motor Manifestations.
- SLUDGE + *Killer Bees*
- DUMBELLS
- IMS (Intermediate Syndrome)
- Organophosphate-induced delayed Neuropathy
- Chronic Exposure: Neusopsychiatric Sx with Cognitive dysfx and Memory loss.
“SLUDGE” and “DUMBBELLS”

- S - Salivation
- L - Lacrimation
- U - Urination
- D - Diarrhea
- G - Gastric Upset
- E - Emesis

- D - Diarrhea
- U - Urination
- M – Miosis /Muscle weakness
- B - Bronchorrhea
- B - Bradycardia
- E - Emesis
- L - Lacrimation
- S - Salivation/Swelling
OPC Diagnosis

- Hydrocarbon / Garlic-like odor.
- Cholinesterase assay.
- Test dose of IV atropine.
- Differential Dx is broad.
- Consider exposure to medicinal cholinergic agents.
- RBC Cholinesterase levels are useful, but not prognostic and DO NOT correlate with the amount of Atropine to be given.
- EMG – quantifies inhibition of NMJ.
OPC Treatment

- ABC’s
- Decontamination (FIRST)
- Prevention of Absorption
- Administration of Antidotes
- Rx should not be withheld pending cholinesterase levels
- Wear Protective clothing upon touching the patient
- Gentle secretions suction
If Airway Protection is needed...

- What intubation agent shall we use for Neuromuscular blockade?
  
  - Non-depolarizing agent:
    
    - Pancuronium
    - Rocuronium
    - Atracurium
    - Vecuronium
    - Mivacurium
Why NOT to use Succinylcholine?

- It is metabolized by the Plasma Cholinesterase and therefore, prolonged paralysis may result.

- ANECTINE®
ANTIDOTES for OPC

- ATROPINE
- PRALIDOXIME

Figure 7-1. Nerve Agent Antidote Kit, Mark I.
ATROPINE

• Competitive antagonist of Ach at CNS and peripheral Muscarinic receptors
• Reverses excessive parasympathetically stimulation
• Initial Test Dose: Adults 1mg and Children 0.01-0.04mg/kg IV or IM
• The dose necessary induce Atropinization may be on the order of HUNDREDS of mgs and prolonged Rx might be necessary.
• Inadequate dosing = Treatment Failure
ATROPINIZATION

• It is present when the patient exhibits:
  1. Dry skin and Mucosa
  2. Decreased or Absent BS
  3. Tachycardia
  4. Reduced secretions
  5. No bronchospasm
  6. Mydriasis

No Clinical Importance !!!
Other Strategies:

- High-dose Diphenhydramine
- Nebulized Atropine
- Inhaled Ipratropium bromide
- Glycopyrrolate
- Even Scopolamine
- **Ativan®** – decreasing CNS Sx

**Atrovent®** and **Robinul®** do not cross the Blood-Brain Barrier and are ineffective in Rx CNS symptoms.
PRALIDOXIME - ONE

- Oximes (compounds)
- Displace OPC from Cholinesterases
- 2-PAM is a specific antidote
- Restores Ach activity and prevents toxicity by detoxifying the remaining OPC molecules
- Some Nerve agents like SOMAN have very quick AGING.
- Ameliorates Symptoms
- If given early (before AGING) reverses Muscle paralysis
PRALIDOXIME - TWO

- Get Blood samples for Blood Cholinesterase levels before Rx
- Can be given for prolonged periods of time (>24 to 48 hrs)
- **Dose:** Adults 1-2 gr and Children 20-40 mg/kg up to 1gr, infused with NS x 30 min IV/IM - Administer ASAP
- Continuous gtt might be needed (200-500mg/hr) titrating to symptoms
- Dymethoxy compounds like Malathion and Methyl demeton seem not to be affected by the Rx with 2 PAM.
The usual cause of death is from Respiratory failure secondary to paralysis of respiratory muscles, CNS depression and Bronchorrhea.

Death usually occurs within 24 hrs in untreated patients. If treated early, and no ischemic hypoxic damage is noted, symptomatic recovery occurs within 10 days of the exposure / ingestion.
Hey—are you thinking what I'm thinking?
Ib. - Carbamates

- TRANIENTLY and REVERSEBLY inhibit the Cholinesterase enzyme.
- Regeneration of Activity is Fast
- Aging DOES NOT occur
- No new enzyme synthesis is required before Normal Function returns.
- Structurally related to OPC.
- Medicinal forms: Physostigmine, Pyrodistigmine and Neostigmine.
Common Carbamates

- Sevin, Baygon, Lannate, Carbaryl, Aldicarb.
- Structurally related to OPCs.
- They DO NOT produce depressed Blood Cholinesterase levels / activity.
Clinical Features

- Similar to cholinergic crisis with OPC but of **shorter duration**.
- Less toxicity is seen due to less CNS penetration, and Sz do not occur.
- More severe in children.
- Could be serious in Massive OD’s.
- Rapid improvement due to Rapid hydrolysis of the Carbamate - Ach bond and quick enzymatic regeneration.
• Symptoms usually resolve without pralidoxime therapy.

“Administration of 2-PAM to a poisoned patient in a Cholinergic crisis is **APPROPRIATE** if it is unknown whether the patient is suffering from OPC or Carbamate pesticide poisoning”.
Ic - ORGANOCHLORYNES

• DDT is the prototype.
• Most of them Banned from the US
• Environmental damage, long half life in Human bodies and Toxicity.
• Most are CNS stimulants.
• DDT discovered in 1940’s
• Where highly effective ‘
• Revolutionized Agriculture.
SOME Common ORGANOCHLORYNESES

- Lindane / Kwell®
- DDT
- Aldrin
- Dieldrin
- Endrin
- Heptachlor
- Toxaphene
- Isobenzan

- Chlordane
- Endosulfan
- Dienochlor
- Chlordecone
- Mirex
- Dicofol
- Chlorbenzilate
- Methoxychlor
Rachel Carson & “Silent Spring”
Rachel Carson & “Silent Spring” – Book Importance

- **In 1962,** she exposed the hazards of the pesticide DDT, eloquently questioned humanity's faith in technological progress and helped set the stage for the environmental movement.

- **Carson,** a renowned nature author and a former **marine biologist** with the **U.S. Fish and Wildlife Service,** was uniquely equipped to create such a startling and inflammatory book.
Toxicity

- Decreases Sodium channel permeability – Rapid Nn discharges
- Highly lipid soluble
- Accumulate in human tissues
- Induce the hepatic microsomal system and interferes with other medications metabolism.
Symptoms

- Mostly Neurologic issues.
- Dizzy, malaise, fatigue, irritability, delirium, HA, tremors, myoclonus, facial paresthesias.
- Fever is common.
- Seizures, coma and Resp. Failure
- Myocardial irritability with arrhythmias
- Chronic Neurotoxic effects.
Id - PYRETHRINS & Pyrethroids

• Naturally occurring botanical substances found in the *Chrysanthemum* plant.

• **Pyrethroids** – Synthetic compounds.

• Effect on Na Channels and GABA receptors.

• Cause Dermal, Pulmonary, GI and Neurologic findings.
Id - PYRETHRINS & Pyrethroids - TWO

- Pyrethrines cross react with Ragweed and could cause Allergic Reactions.
- Contact dermatitis
- **Elemite®** / Permethrin – SCABIES.
- Airway irritation – Asthma attacks.
- In severe poisoning multiple diffuse manifestations could occur.
- Disposition is based on Severity of the asthmatic / allergic manifestations.
Deep Woods OFF!®

Long Lasting Protection

Repels Mosquitoes That May Carry West Nile Virus
Ie - DEET / OFF®

- Used extensively – OTC
- Concentrations from 5 to 100%
- Absorbed through the skin
- Unknown mechanism of Toxicity
- Sx: Restlessness, Confusion, AMS, even Seizures.
- Most exposures are local irritation
- Supportive care
- AAP recommends DEET concentrations of less than 10% (OTC 5-7%).
- Avoid use in abrasions / denuded skin
**EPIDEMIOLOGY**

- AAPCC / NPDS reports 34’786, of those 11’683 were exposures to long acting anticoagulants per year.
- Most often due to the 4-hydroxycoumarins: Brodifacoum, Difenacoum and the Indione derivatives Chlorphacinone.
- Mostly asymptomatic.
- 1493 cases in adults a year with significant Coagulopathy.
- 85% in children < 6 years old.
Classification - ONE

- Non Anticoagulant
  1. High Toxicity
     - Arsenic
     - Barium
     - Phosphorus
     - PNU
     - Sodium monofluoroacetate
     - Strychnine
     - Thallium
     - Zinc Phosphide

- Non Anticoagulants
  2. Moderate Toxicity
     - Naphthylthourea
     - Cholecalciferol
  3. Low Toxicity
     - Bromethalin
     - Norbomide
     - Red squill
Classification – TWO
Anticoagulants

- Short Acting
  - Warfarin: Interferes with clotting factors II, VII, IX, X.
  - Prolin: + antibiotic combination that eliminates intestinal Vit K producing organism.

- Long Acting
  1. Hydroxycoumarins
     - Brodifacoum
     - Difenacoum
  2. Indandiones
     - Pindone
     - Pivalyn
     - Diphacionone
     - Valone
     - Chlorphacinone
Arsenic

- No longer used – Highly toxic.
- Quick onset of Symptoms.
- Death: CV collapse within 24 hrs
- Tx: Charcoal, lavage, catharsis
- DMSA / Succimer – Dimercaprol chelation therapy
- Penicillamine.
Barium carbonate

- Highly Toxic compounds.
- Neuromuscular blockade noted with Hypokalemia and Paralysis.
- Tx: OG lavage with Sodium or Magnesium sulfate to convert carbonate to a less toxic sulfate and K replacement.
Elemental or Yellow / White Phosphorus

- Garlicky odor – 50mg are fatal.
- Can cause severe skin irritation.
- Uncouples oxidative phosphorylation
- Cardio / Nephro and Angiotoxic.
- Sx: Oral Burns, Abd pain, GI bleed
- “Smoking” luminescent Vomit and stool – Red Phosphorus: Relatively harmless if ingested (Matches).
PNU / Vacor or N-3-Pyridylmethil-N’-p-nitrophenylurea

- Out of the Market / Historical importance.
- Interfered with Pancreatic Nicotinamide Metabolism.
- Destroyed β-Cells of the Pancreas.
- Sx: Hyperglycemia and Ketosis with remarkable Neuropathies.
- Tx: IV / IM Nicotinamide / Insulin.
- Is providing new insight into environmental etiologies for Dz: DM.
STRYCHNINE

- Highly Toxic / Cathartic
- Naturally occurring
- *Strychnis nux-vomica* tree seeds
- Used in the 16th century
- CNS stimulant
- Is not an effective rodenticide: Rats learned to avoid its bitter taste.
- Not used Anymore
Thallium sulfate

- Heavy Metal / Homeopathic remedies
- Common in Homicides and Suicides
- Cumulative poison
- Interferes with Oxidative phosphorylation
  Measured in hair, serum, urine
- K chloride infusions needed
- **Prussian Blue** (K ferric hexanocyanate) may interrupt enterohepatic circulation and decrease absorption.
Zinc phosphide

- Rotten fish odor
- Phosphine gas released @ H2O or acid contact --- Inhalation issues.
- Widespread Cellular toxicity
- Inhibit cytochrome oxidase and electron transport system.
- Injury and Necrosis to the GI tract, liver and kidneys.
- Tx: Dilution with Na Bicarb, milk, water and PPI and Antacid.
- Chronic occupational exposure – Found in grain Elevators.
Cholecalciferol (Vitamin D3)

- Professional Exterminators usage
- No severe human toxicity reported
- Toxic doses: Hypercalcemia, Osteomalacia, Calcifications.
- Monitor Serum Ca, Mg, and Electrolytes.
- Tx (Hypercalcemia) with IVF, Lasix, steroids, calcitonin, biphosphonates.
Low Toxicity agents

- **Bromethalin**: Newer agent, neurotoxic, and Limited experience in humans. Tx: BDZ and Supportive.

- **Norbormide / Dicarboximide**: No known Human Toxicity, Supportive.

- **Red squill**: Botanic Glycoside, has Digoxin-like activity. Consider Digoxin levels and Rx with Anti-Fab (Digibind®). Cardiotoxic.
Anticoagulants

“Most one-time Warfarin ingestions are insignificant and accidental poisonings and do not cause bleeding issues”

“Toxicity requires large amounts in a single exposure or repetitive exposure over several days”
Warfarins

- First anticoagulant Rodenticides
- Half life is 42 hrs.
- Baseline INR repeated q12-24 hrs.
- Rx with Phytonadione (Vit K1).
- Toxic oral dose: >5 to 20mg per dose x more than 5 days.
- Onset 12 to 48 hrs after ingestion.
- Activated charcoal / cathartic.
Inandione Derivatives
(2\textsuperscript{nd} Generation Anticoagulants)

- Introduced due to Rodent resistance to Warfarin.
- Responsible for 80\% of human exposures in the U.S.
- Same Mechanism of Activity
- More potent with Prolonged activity
- Potential for High toxicity
- Pindone, Diphacinone, Valone, Chlorphacinone – similar to superwarfarins
Superwarfarins
(4-Hydroxy-coumarins)

- Half Life is aprox. Close to 120 days
- A single ingestion will result in marked anticoagulation – Charcoal / Cathartic.
- Will last for months – Chronic Rx.
- Baseline CBC / INR / Factors II and VII assays and Serum assays for:
  * Brodifacoum
  * Diphenacoum
  * Coumafuryl
  * Bromadiolone
- Symptoms within 24 hrs
- High dose Oral Vitamin K1
- For Acute Bleeding --- FFP Transfusions.
IMPORTANCE - ONE

- Chemicals used to Kill Weeds
- Still impose a Health hazard despite their low toxicity in mammals.
- Inhibit plant photosynthesis, respiration, protein synthesis or growth stimulation.
- Mimic plant Hormones: AUXINS
- Toxic ingredients: Organic solvents, Surfactants, Preservatives.
IMPORTANCE - TWO

- Are among the best-studied chemicals in Modern society.
- Prototypes: PARAQUAT / DIQUAT
- 180 Chemicals registered in the U.S.
- Account for 40% of the Worldwide pesticide use (5.86 billion pounds).
- USA x 25% of world Herbicide use.
- Largest use: Agriculture (83%).
Classification

- **Chlorophenoxy Herbicides:**
  2,4-D / MCPA / 2,4,5-T and TCDD
  Agent Orange – applied during Vietnam

- **Bipyridyl Herbicides:**
  Paraquat and Diquat – Huge Morbidity.

- **Urea-substituted Herbicides:**
  Chlorimuron, Diuron, Fluometron

- **Organophosphorus Herbicides:**
  Butiphos
PARAQUAT

- Safe when used as directed
- Dramatic Toxicity when misused
- Low cost
- Rapid action
- Environmentally favorable
- Remains widely used across the World
TOXICITY - One

- From: Solvents, Surfactants, Emulsifiers, Preservatives, Adjuvants
- Regulations in the U.S. about the public and environmentally toxic inert ingredients.
- EPA / Inerts Regulatory Strategy.
- In emergencies:
  “Any material Claimed to be a Trade Secret must be revealed immediately upon request” --- with some Exceptions!!!
TOXICITY - Two

- Most cases are Deliberate ingestions
- Thousands of Deaths
- Homicidal use, massive transdermal exposure, IV administration, prolonged occupational spraying.
- Once the Free radical-initiated pulmonary fibrosis is under way, even heroic medical measures fail to salvage the patient.
Symptomatology from Paraquat

- Severe Caustic effects
- Severe Corrosive corneal damage
- Upper Resp. Tract injury / Epistaxis
- Inhalation: Cough, CP, Pulm. edema and Hemoptysis.
- Acute Lips and Mouth ulceration – caustic lesions (Pseudo diphtheria)
- Renal failure = Heralds poor prognosis.
- Hepatocellular necrosis
- Mortality as HIGH as 75%.
- Outcome is Dose-dependent.
Management

- Any patient exposed to Paraquat, shall be treated as a True Emergency
- Even if there are no Symptoms.
- Spontaneous Vomiting (emetic added formulations).
- Slurry of Activated charcoal
- **EAT Fuller’s earth, Bentonite or Garden Clay** – if there will be delay in reaching the Hospital.
Adsorbents

- Fuller’s earth in a 15% aqueous suspension.
- Bentonite in a 7% aqueous slurry.
- Activated Charcoal 1 to 2 gr/kg.

With Cathartic: SORBITOL 70% (2ml/kg)
DIQUAT

- Mixed with Paraquat is several formulations
- Kills aquatic weeds
- Similar toxicity to Paraquat
- Caustic to skin and GI tract.
- Renal and Liver necrosis.
- Mortality approaches 50%.
GLYPHOSATE

- Synthesized by a **French** and posted in a Chemical bank in the 1960’s.
- An **American** company acquired it and discovered the remarkable herbicidal activity
- Widely used WW.
Toxicity / Therapy

- Main culprit = **Surfactant**.
- Toxic Syndrome remains controversial
- Agricultural Surfactant Sx / poisoning
- No specific antidotal measures.
- Fatalities occur 2 days after ingestion.
- **Sx:** Respiratory distress, failure, intubation, Renal failure with HD, and finally irreversible shock.
- Wide range of Clinical symptoms have been described in the Literature.