Toxicology of Agricultural Pesticides

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Learning Objectives

- **1.** Discuss acute & chronic health effects of pesticide exposure

- **2.** Prioritize the major categories of pesticides based on their acute toxicities

- **3.** Review cholinesterase testing in the diagnosis and prevention of organophosphate toxicity

Definition - EPA

"...a pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest"

"…a pest is any harmful, destructive, or troublesome animal, plant or microorganism"

US Environmental Protection Agency (EPA)

Classes of Pesticides

- Insecticides (kill insects)
  - Organochlorines
  - Organophosphates
  - Carbamates
  - Pyrethrins/pyrethroids
  - Neonicotinoids
- Herbicides (kill plants)
- Rodenticides (kill rodents)
- Fungicides (kill fungus)
- Fumigants (kill whatever)

2023 Nebraska Poison Center Pesticide Exposure Calls

Class	Number	Percent
Insecticide	701	62.0
Herbicide	168	14.9
Rodenticide	127	11.2
Repellant	104	9.2
Fungicide	30	2.6
Fumigant	1	0.1
Total	1131	100.0

Insecticides accounted for 62% of pesticide calls to NPC in 2023

2023 Nebraska Poison Center Insecticide Exposure Calls

Class	Number	Percent
Pyrethroid	276	39.4
Pyrethrin	43	6.1
Organophosphate	27	3.9
Carbamate	12	1.7
Borate	192	27.4
Neonicotinoid	1	0.1
Other	107	15.3
Unknown	43	6.1
Total	701	100.0

45.5% of insecticide calls were for pyrethrins and pyrethroids

More toxic OPs and carbamates accounted for just 5.6%

Case 1

- 39-year-old man was spraying insecticide on his employer's property (not his regular job)
- Diluted diazinon 4 oz into 1 gallon
  - Sprayed x 2.5 h with break for lunch
  - Used leather work gloves
  - No other PPE; wore shorts & T-shirt
- Became dizzy with N/V, diarrhea, blurred vision, muscles spasms, diaphoresis
- A friend drove him home
- Symptoms didn't improve with shower

Adverse Effects of Pesticide Use

- Contamination of air, water, food supply
- Proliferation of resistant species
- Injury to non-target species
- Injury to humans
  - Pesticide handlers, applicators
  - Agricultural communities
  - General public
  - Children may be more vulnerable
- Acute poisoning better characterized than effects of chronic exposure

Early Pesticide History

- 1600s – Strychnine extracted from S. Asian plant and used to kill rodents
- Late 1600s – Nicotine extracted from tobacco leaves and sprayed on plants as insecticide
- 1800s – Pyrethrum extracted from chrysanthemum as an insecticide

Strychnos nux vomica plant

Nicotiana tabacum

Pesticides in Recent History

- Organophosphate (OP) insecticides and nerve agents developed in Germany, 1930s
- After WW II, OPs & DDT introduced into agriculture
- Other organochlorines came into use, phased out in 1950s
- Organophosphate use declined in 1980s
- Pyrethroids became increasingly important in 1960s
- Pheromones, chitin inhibitors, neonicotinoids and others came into use 1980s - 2000s

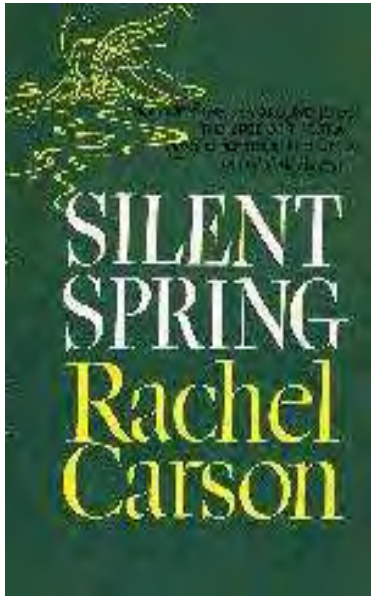
Recent history (cont'd)

- In 1940s and 50s, synthetic pesticides were widely regarded as beneficial and harmless

1940s advertisement Taylor, Southern Regional Extension Forestry, March 2007

Silent Spring (1962) warned of the ecologic threat from persistent organochlorine insecticides

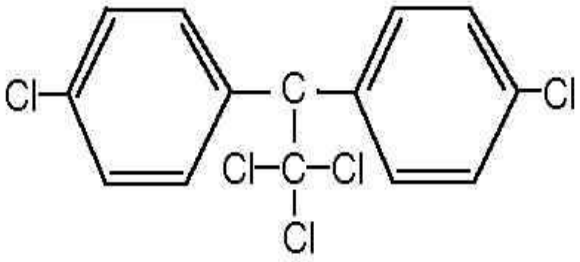
Rachel Carson, 1907-1964



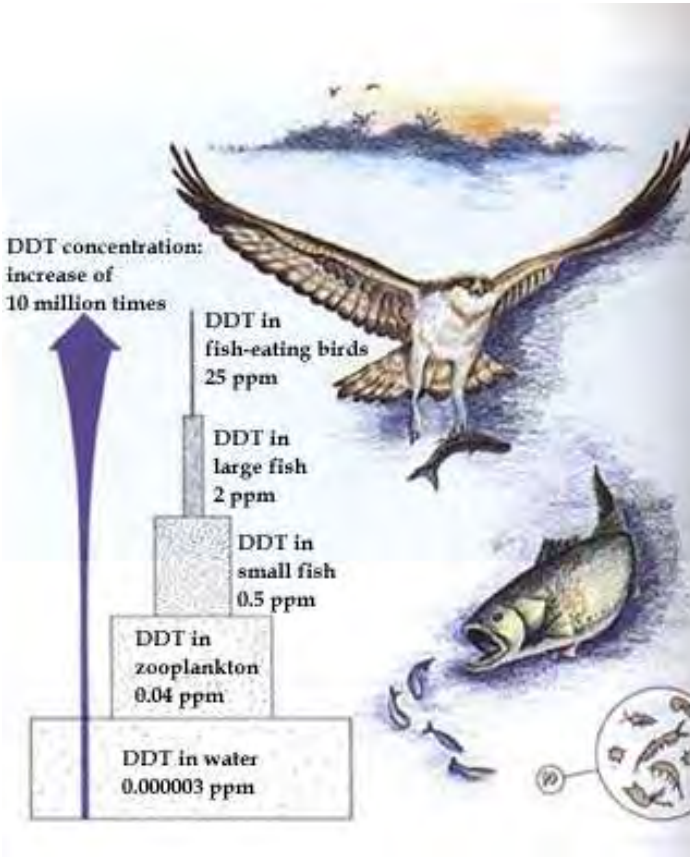
Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
1947, with updates 1972, 1975, 1975, 1988, 1996, and 2012 - Pesticides classified as general use or restricted use (by licensed or certified applicators)

Insecticides: Organochlorines

- DDT and analogues
- Introduced during WW II, effective against malaria-carrying mosquitoes and crop pests
  - Neuroexcitation via Na channels
  - Long persistence in environment (and body)
  - Concentrated up food chain
  - Banned in US 1972
    - Lindane still available for ectoparasites
  - DDT still used in developing world



p,p' Dichlorodiphenyltrichloroethane

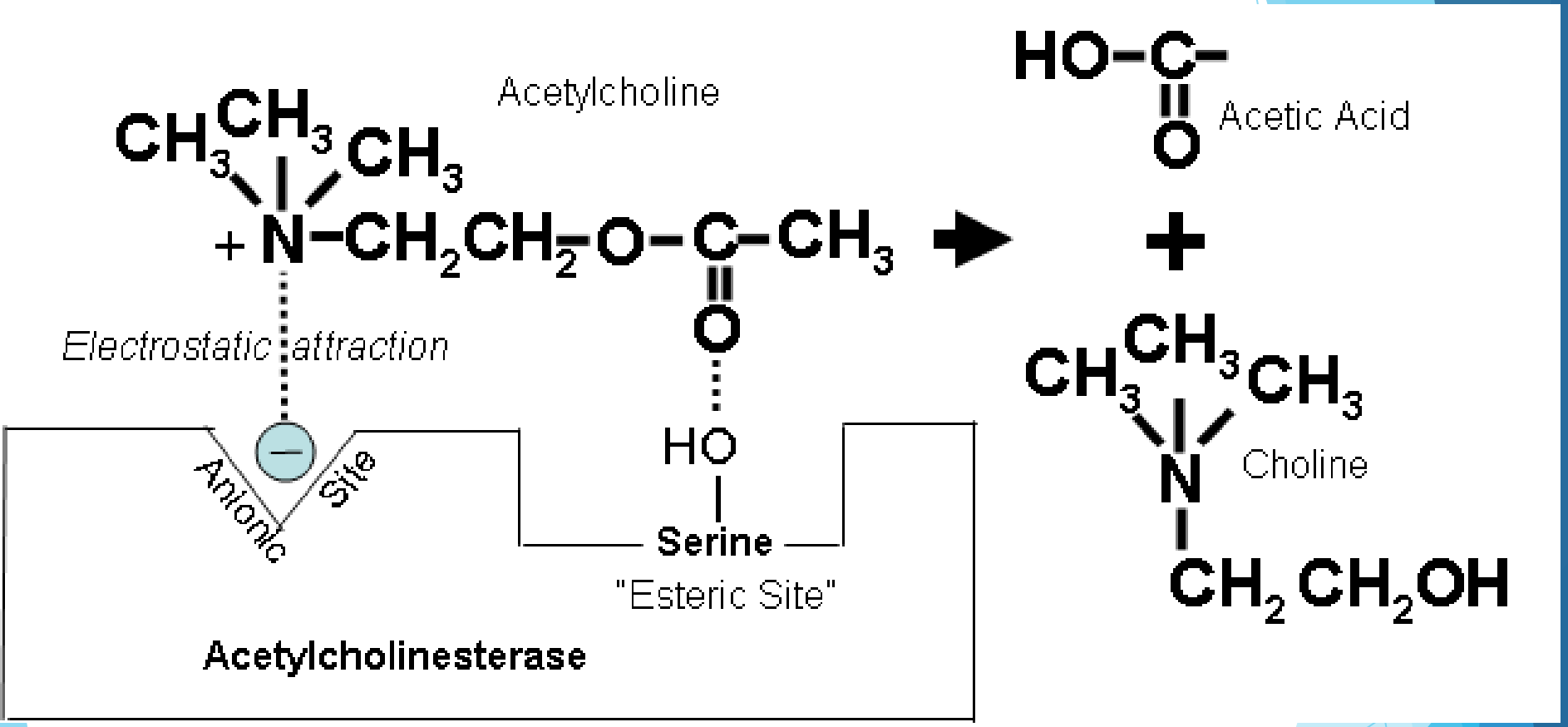


Insecticides: Cholinesterase Inhibitors

- Inhibit breakdown of neurotransmitter acetylcholine
- Some are highly toxic but less persistent in environment than organochlorines
- Organophosphates (aka organic phosphorus compounds)
  - Irreversible inhibitors
  - Leading cause of poisoning fatality worldwide (mainly in developing world) estimated at 100,000 annually (1)
- Carbamates
  - Reversible

1. Eddleston, 2019

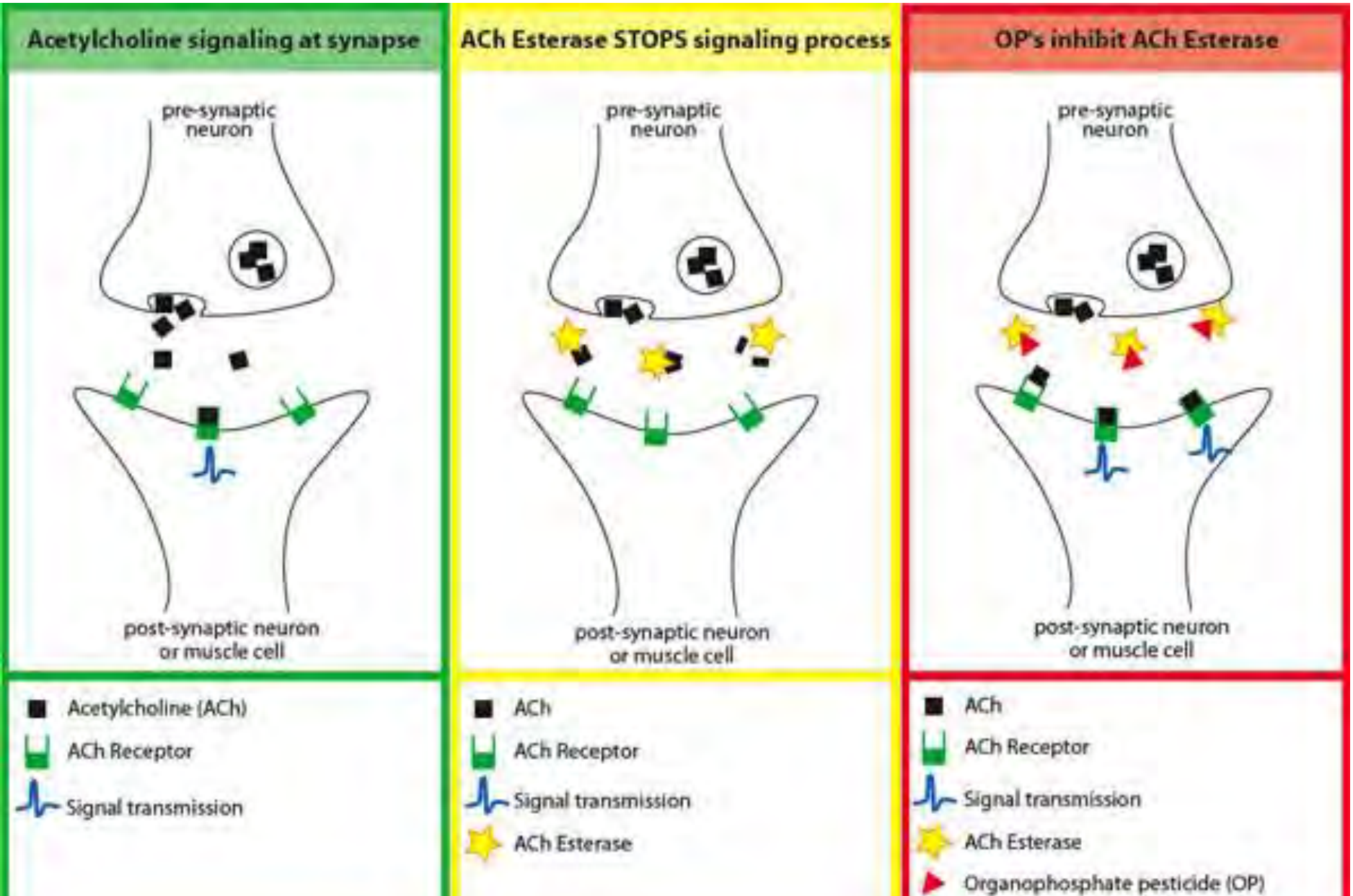
Acetylcholinesterase mechanism



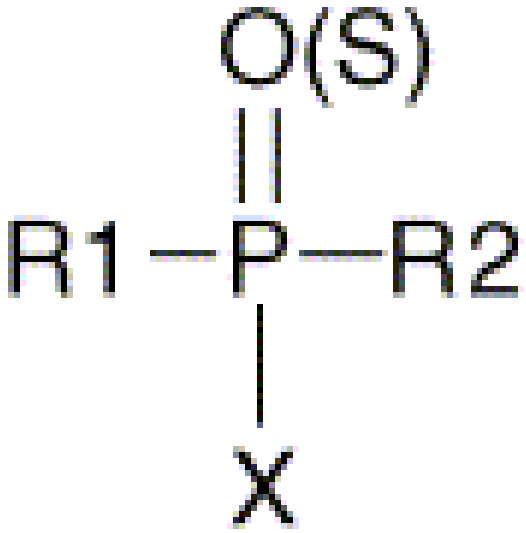
After interacting with receptor, ACh is rapidly broken down by AChE

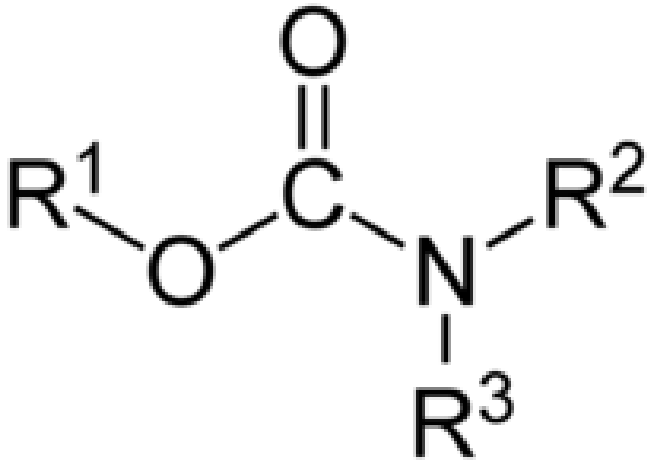
Choline is taken back into neuron and reused

OP/carbamate MOA



Structure of OPs & carbamates





Carbamate structure

General structure of organophosphate insecticide
X = leaving group

If P is double bonded to S (thion) it must be converted to active (oxon) form (P = O)

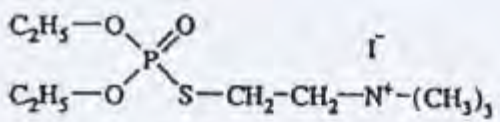
Examples of OP insecticides

COMMON NAME	PRODUCT EXAMPLE	CHEMICAL NAME	ESTIMATED FATAL ORAL DOSE (g/70 kg)
Agricultural Insecticides (high toxicity)			
Tetraethyl pyrophosphate	Miller Kilmite 40	Tetraethyl pyrophosphate	0.05
Phorate	Thimet (American Cyanamid)	*0,0,*-Diethyl (*S*-ethylmercaptomethyl) dithiophosphate	
Parathion	Niagara Phoskil Dust	*0,0,*-Diethyl-*0*-*p*-nitrophenyl phosphorothioate	0.1
Phosdrin	Mevinphos (Shell)	Dimethyl-0-(1-methyl-2-carbomethoxy-vinyl) phosphate	0.15
Disulfoton	Disyston	Diethyl-*S*-2-ethyl-2-mercaptoethyl phosphorodithioate	0.2
Animal Insecticides (intermediate toxicity)			
Coumaphos	Co-Ral Animal Insecticide	Diethyl-*0*-(3-chloro-4-methyl-7-coumarinyl) phosphorothioate	
Chlorpyrifos (Dursban)	Rid-A-Bug (Kenco)	*0,0*-Diethyl-*0*-(3,5,6-trichloro-2-pyridyl) phosphorothioate	
Trichlorfon	Trichlorfon Pour On (Hess & Clark)	Dimethyl trichlorohydroxyethyl phosphonate	
Ronnel	Korlan Livestock Spray (Dow)	*0,0*-dimethyl-*0*-(2,4,5-trichlorophenyl) phosphorothioate	
Household Use or Golf Course/Community Spray (low toxicity)			
Diazinon	Security Fire Ant Killer (Woolfolk)	Diethyl-*0*-(2-isopropyl-4-methyl-6-pyrimidyl) phosphorothioate	25.0
Malathion	Ortho Malathion 50 Insect Spray	Dimethyl-*S*-(1,2-bis-carboethoxy) ethyl phosphorodithioate	60.0
Vapona (dichlorvos, DDVP)	Shell No-Pest Strip	*0,0*-Dimethyl-*0*-2,2-dichlorovinyl phosphate	
Acephate	Chevron Orthene	*0,S*-Dimethylacetylphosphoramidothioate	

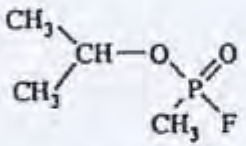
Haddad & Winchester's Clinical Management of Poisoning and Overdose 4th ed, 2007

Classification of OPs

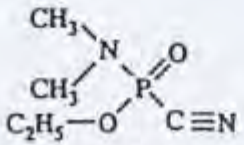
- Group 1–phosphorylcholines
  - Leaving group: substituted quarternary nitrogen
  - Echothiophate iodide
- Group 2–fluorophosphates
  - Leaving group: fluoride
  - Dimefox, sarin, mipafox
- Group 3–cyanophosphates, other halophosphates
  - Leaving group: CN-, SCN-, OCN-, halogen other than fluoride
  - Tabun
- Group 4–multiple constituents
  - Leaving group:
  - Dimethoxy
    - Azinphos-menthyl, bromophos, chlorothion, crotoxyphos, dicapthon, dichlorvos, dicrotophos, dimethoate, fenthion, malathion, mevinphos, parathion-methyl, phosphamidon, temephos, trichlorfon
  - Diethoxy
    - Carbophenothion, chlorfenvinphos, chlorpyriphos, coumaphos, demeton, diazinon, dioxathion, disulfoton, ethion, methosfolan, parathion, phorate, phosfolan, TEPP
  - Other dialkoxy
    - Isopropyl paraoxon, isopropyl parathion
  - Diamino
    - Schradan
  - Chlorinated and other substituted dialkoxy
    - Haloxon
  - Trithioalkyl
    - Merphos
  - Triphenyl and substituted triphenyl
    - Triorthocresyl phosphate (TOCP)
  - Mixed substituent
    - Crufomate, cyanofenphos



Echothiophate iodide



Sarin



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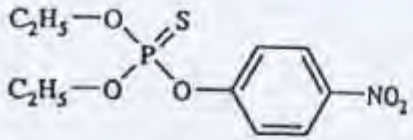
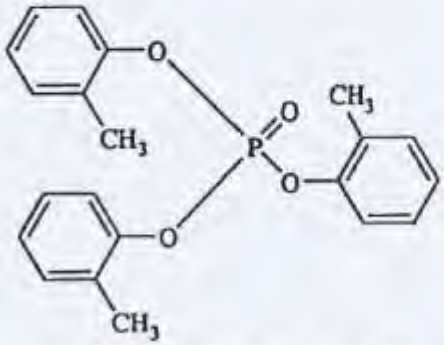


Parathion

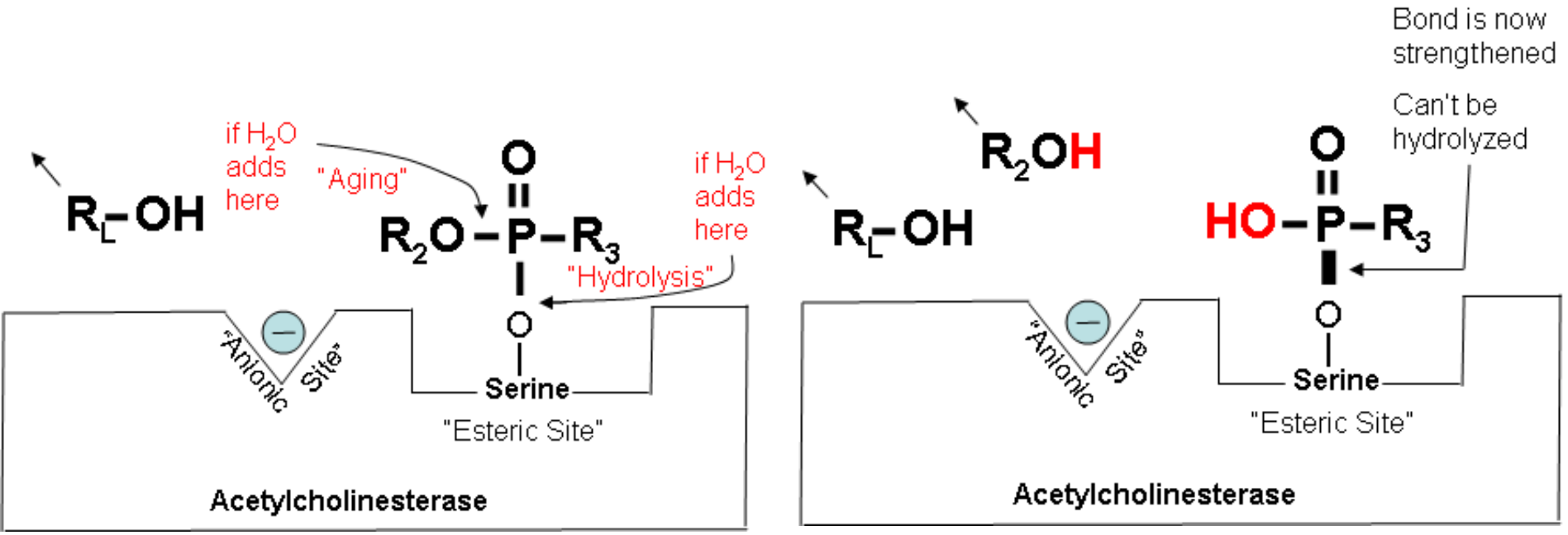


Triorthocresyl phosphate (TOCP)

Kinetics largely determined by structure of R-groups

Source: *Goldfrank's Toxicologic Emergencies* 11th edition, 2019

‘Aging’ of organophosphate



A: OP is bonded to AChE, but bond can be hydrolyzed regenerating the enzyme

B. After ‘aging’ bond can’t be broken - new enzyme must be synthesized → prolonged recovery

Aging T ½ varies greatly from ~ 3 h for dimethoxy OPs (fenthion) to ~ 30 h for diethoxy compounds (parathion)

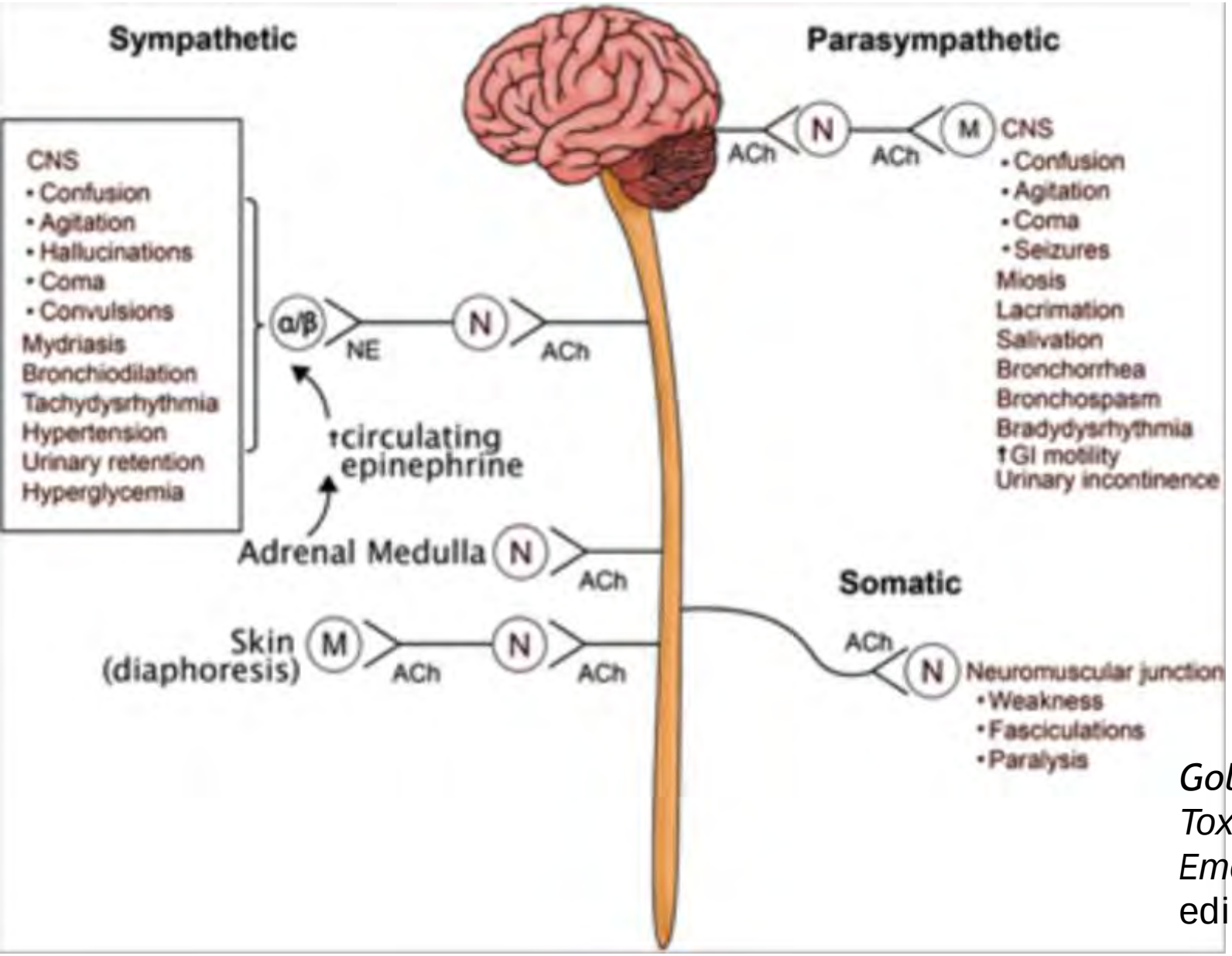
OP pharmacokinetics

- Most are lipophilic
- Well absorbed from lung, skin, GI tract
  - Onset of effects most rapid with inhalation
  - Least rapid with dermal absorption
- Some are metabolized to active compound
- Most OPs rapidly distribute from serum to tissue and fat
  - Redistribution from fat and ‘aging’ can result in prolonged effect

OP/carbamate pathophysiology

- AChE inhibition → ACh stimulation at muscarinic and nicotinic receptors in CNS, PNS, NMJ
- Prolonged stimulation at muscarinic receptors → salivation, diaphoresis, bronchorrhea, etc
- Prolonged stimulation at NMJ nicotinic receptor → initial muscle activity (fasciculations), then desensitization and paralysis
- OP AChE inhibition is irreversible after aging
- Carbamates don't age - AChE inhibition is reversible

OP: Acute toxicity



Goldfrank's Toxicologic Emergencies 11th edition, 2019

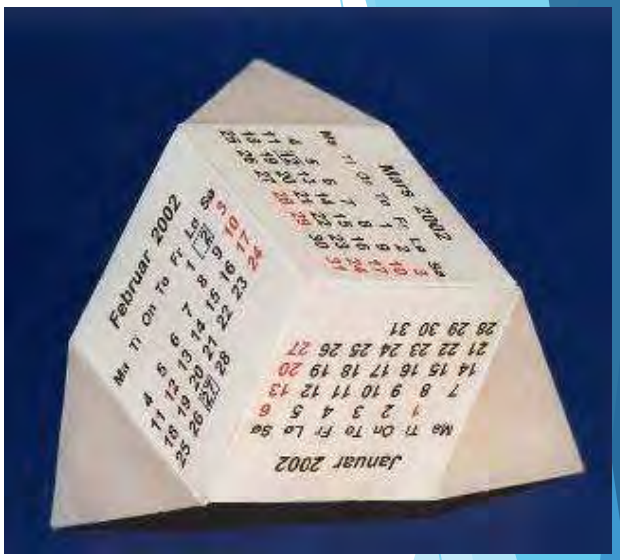
OP/Carbamate mnemonics

- Muscarinic effects (“wet” signs/symptoms)
  - D diaphoresis, diarrhea
  - U urination
  - M miosis
  - B bronchorrhea, bronchospasm
  - B bradycardia
  - E emesis
  - L lacrimation
  - S salivation
- Diaphoresis, bronchorrhea, and miosis are most reliable signs

”

OP/Carbamate mnemonics (cont'd)

- Nicotinic effects
  - M mydriasis
  - T tachycardia
  - W weakness
  - Th tremors, hypertension
  - F fasiculations
- CNS effects
  - C confusion
  - C coma
  - C convulsions
- Opposing muscarinic & nicotinic effects seen for some exam findings (HR, pupil size)



Severity of Poisoning

MILD

- Walks & talks
- Headache & dizzy
- Nausea, vomiting, diarrhea
- Abdominal pain
- Sweating
- Salivating
- Cholinesterase ~30%-50% of normal

MODERATE

- Can't walk
- Soft voice
- Muscle fasciculations
- Small pupils
- Cholinesterase~ 10%-30% of normal

SEVERE

- Unconscious
- No pupillary reflex
- Fasciculations
- Flaccid paralysis
- Increased bronchial secretions
- Resp failure
- Cholinesterase <10% of normal

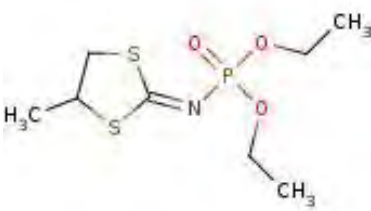
Delayed syndromes

- Intermediate Syndrome
  - Historically a/w OP toxicity but has been reported with carbamates (1)
  - Weakness 1-4 d after exposure without muscarinic signs/symptoms of cholinergic crisis
    - Typical patient can't lift head off bed
  - Thought to be from down-regulation of nicotinic ACh receptors at NMJ
  - Treatment is supportive care

1. Indira, *Clin Toxicol* 2013

Delayed syndromes (cont'd)

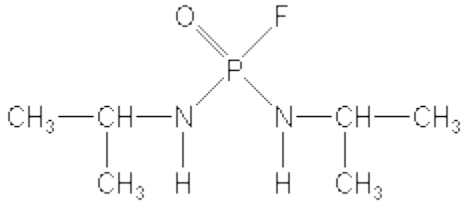
- Organophosphate induced delayed peripheral neuropathy (OPIDN)
  - Rare - seen with triaryl (TOCP) & some dialkyl phosphates (chlorpyrifos, mephosfolan, mipafox)
    - Inhibition of neuropathy target esterase (NTE)
    - Degeneration of long axons → muscle weakness (LE > UE) and pain 2-3 wks post-exposure or later
    - Large distal neurons especially vulnerable
    - May not have had clinical cholinergic toxidrome
    - Atropine & pralidoxime not effective
    - Variable recovery over months to years
    - Very rarely seen with carbamates

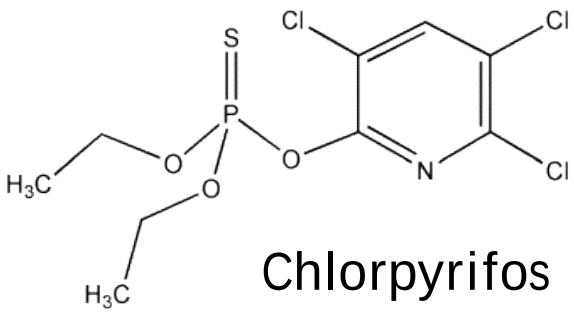


Mephosfolan

Jakonovic, *Clin Neurol Neurosurg* 2011

Mipafox





Chlorpyrifos

Other long term OP effects

- Among pesticide applicators cognitive and mood disturbance a/w long term use of OP & OC insecticides (1)
- After mistaken indoor application of diazinon a family continued to have cognitive and mood changes 3 y later (2)
- Mechanism of long-term CNS effects is not well understood

1. Kamel, *Hum Exp Toxicol* 2007
2. Dahlgren *Clin Toxicol* 2004

OP toxicity: Diagnostic tests

- RBC cholinesterase
  - Better reflection of synaptic inhibition
  - Regenerates more slowly than neuronal AChE
  - ↓ in anemia, but can be adjusted for hemoglobin
  - Send out to reference lab
- Plasma cholinesterase (aka pseudocholinesterase)
  - Falls first
  - Recovers rapidly (days)
  - More daily variation
  - Affected by other conditions
    - Liver dysfunction
    - Malnutrition
    - Pregnancy
  - Easier to obtain

If toxicity suspected, treatment is started while tests are pending

Essentials of Cholinesterase Screening

- General objectives for ChE screening
  - 1) Monitor for exposure (surveillance) and
  - 2) Establish baseline for diagnosis of poisoning in at risk populations.
    - Initially >2 months after potential exposure (during winter)
  - 3) Retest during exposure (planting season)
    - Follow up testing at peak of exposure season
    - Follow up should be same procedure/same lab
    - 20% ↓ in ChE activity from baseline suggests overexposure & need to change in work practices
    - ≥ 30% ↓ in ChE activity - immediate removal from further exposure

https://oehha.ca.gov/pesticides/california-medical-supervision-program

Cholinesterase Inhibitor Treatment

- Airway management as needed
  - Intubation/mechanical ventilation as needed
  - Respiratory failure is most common cause of death
- Decontamination
  - Protect Providers
    - Gloves (rubber or nitrile)
    - Bag clothing
  - Skin
    - Triple wash - soap/water
  - GI decon for intentional ingestion
    - Gastric aspiration if very early presentation
    - Activated charcoal unlikely to be helpful

Cholinesterase Inhibitor treatment (cont'd)

- Antimuscarinic Agents
  - Atropine
    - Adults: Bolus 1-2 mg q 2-15 min
      - Children: 0.02 mg/kg, minimum dose 0.1 mg
    - Double dose if no response in 3-5 min
    - Titrate to dry pulmonary secretions & ↑ HR to ≥ 80
      - Maintenance infusion (~10% reversal dose/hour)
- Oximes (for suspected OP)
  - Pralidoxime (2-PAM, Protopam)
    - 30 mg/kg loading dose over 15-30 min
    - 8-10 mg/kg/h infusion (Children 10-20 mg/kg/h) infusion
- Diazepam or other benzodiazepine for seizures

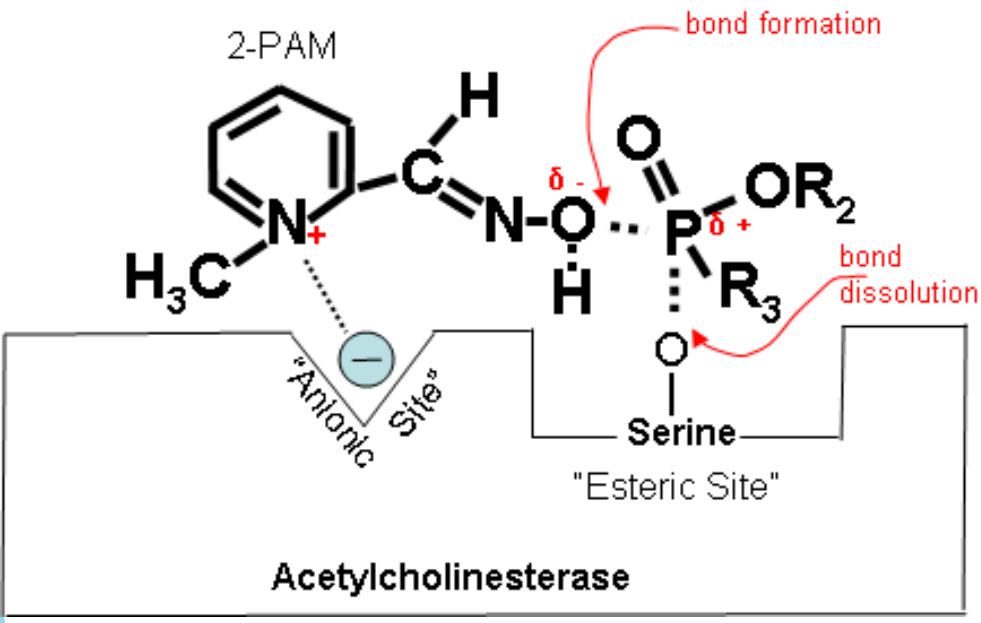
Howland, 2019

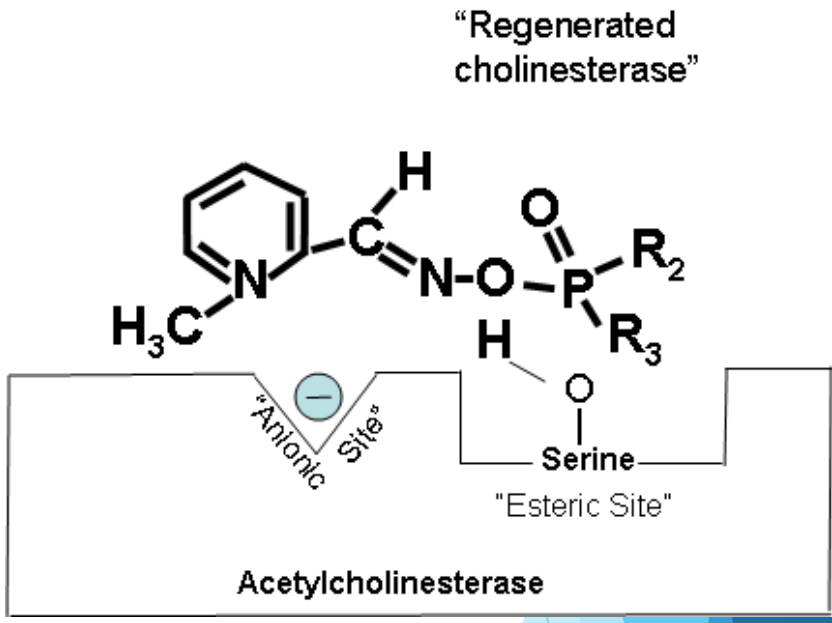
AChE Inhibitor treatment (cont'd 2)

- Initially can use Mark I kit (separate atropine 2 mg & pralidoxime 600 mg autoinjectors)

- Or Duodote (single atropine/pralidoxime 2.1/600 mg autoinjector)
- Poison Center can assist in obtaining kits

Pralidoxime MOA

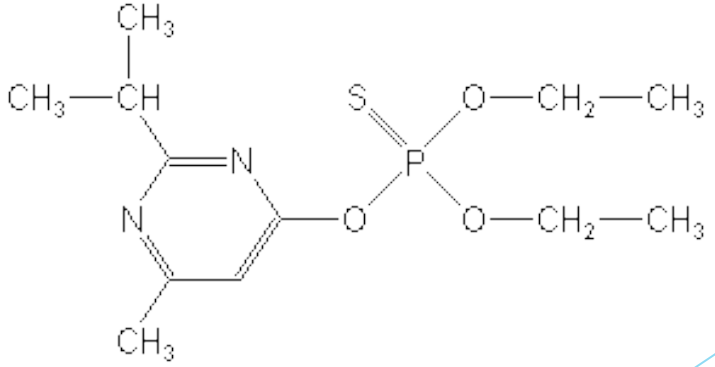




AChE is restored if aging has not yet occurred
After pralidoxime treatment, AChE can still be re-poisoned by OP released from fat stores
Some OPs respond to pralidoxime better than others

Case 1 Conclusion

- 39-year-old spraying employer's property
- In ED BP 136/70, P 87, R 16, T 97.0, O_2 sat 97% on NC oxygen
- Treated with atropine
- Plasma cholinesterase 230 U/L (normal 8,000-19,000) or < 3% of normal
- Pralidoxime started ~ 24 h after exposure & continued for 24 h
- Discharged, but 2 d later c/o persistent weakness & muscle cramping



Organophosphates declined as a proportion of insecticides used in US, 2000-2012

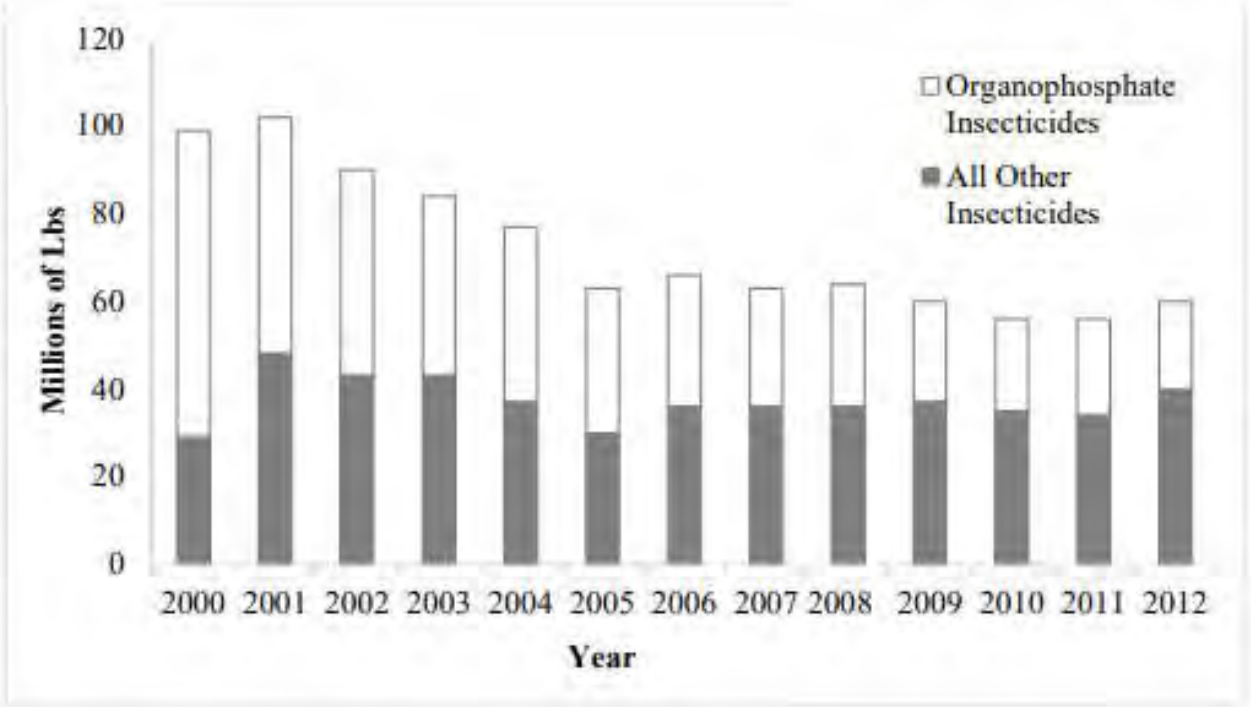


Figure 3.3. Total Amount of Organophosphate and All Other Insecticide Active Ingredients Usage in the United States in All Market Sectors, 2000–2012

Source: Agricultural Market Research Proprietary Data (2000-2012).
Non-Agricultural Market Research Proprietary Data (2000-2012)
USDA/NASS Quick Stats (*http://www.nass.usda.gov/Quick_Stats/*)

Source: EPA.gov

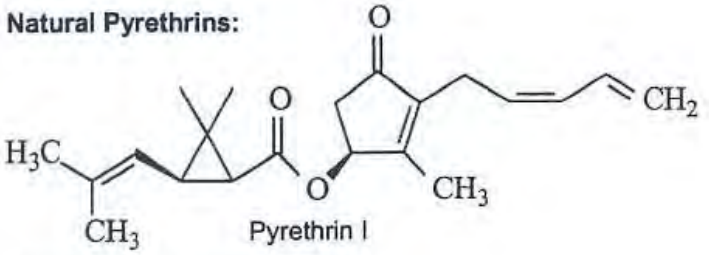
Insecticides: Pyrethrins/Pyrethroids

- Pyrethrins
  - Naturally occurring
  - Derived from Chrysanthemum
  - Neuronal Na channel activation
  - Rapid breakdown in environment
- Pyrethroids
  - Synthetic derivatives
  - Longer persistence
  - More potent

Structures of some pyrethrins and pyrethroids

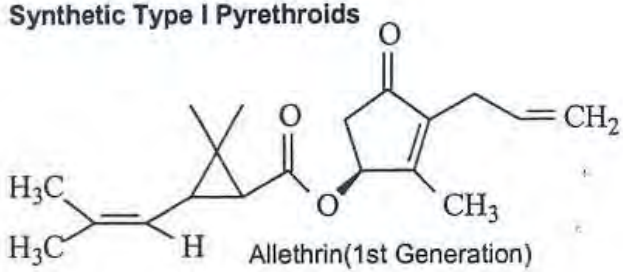
Permethrin
Used topically for lice, scabies
Widely used to spray for mosquitoes during West Nile Virus outbreaks
Most insecticides sold for home use are pyrethroids

Natural Pyrethrins:

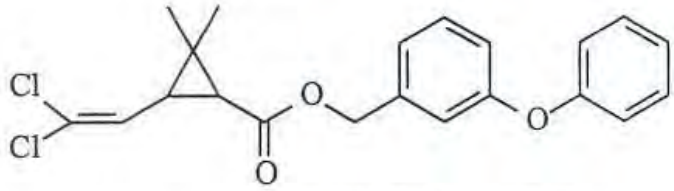


Pyrethrin I

Synthetic Type I Pyrethroids

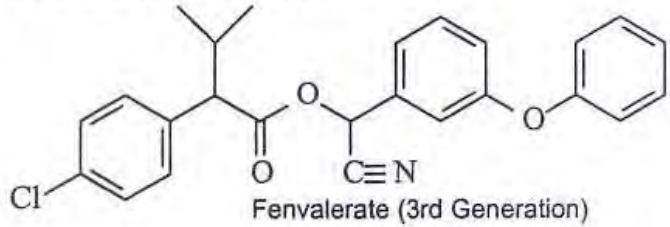


Allethrin(1st Generation)

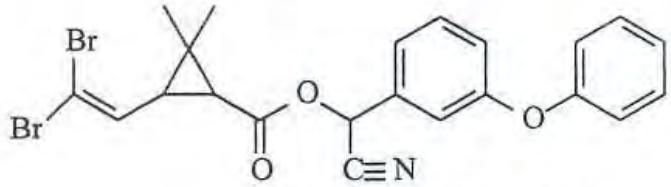


Permethrin (3rd Generation)

Synthetic Type II Pyrethroids



Fenvalerate (3rd Generation)



Deltamethrin (4th Generation)

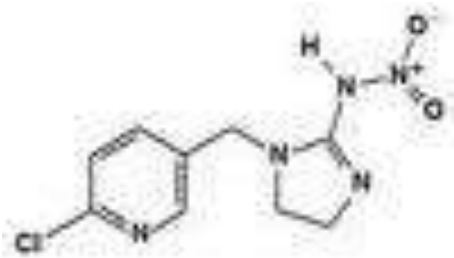
Pyrethrin/pyrethroid toxicity

- Neurostimulation by prolonging Na channel opening
- Much more toxic to insects than humans
- Absorbed orally & by inhalation (aerosols)
  - Minimal systemic absorption through skin
  - Metabolized by CYP enzymes; no bioaccumulation
- Allergic rxns to pyrethrins (esp if allergic to ragweed)
- Type I less toxic - T syndrome (predominant tremors)
- Type II more toxic to humans - C/S syndrome (choreoathetoid movements/salivation)
  - Skin irritation
  - Paresthesias from local effects on cutaneous nerves
- CNS ↓, seizure, and lung injury with large ingestions

Pyrethrin/pyrethroid treatment

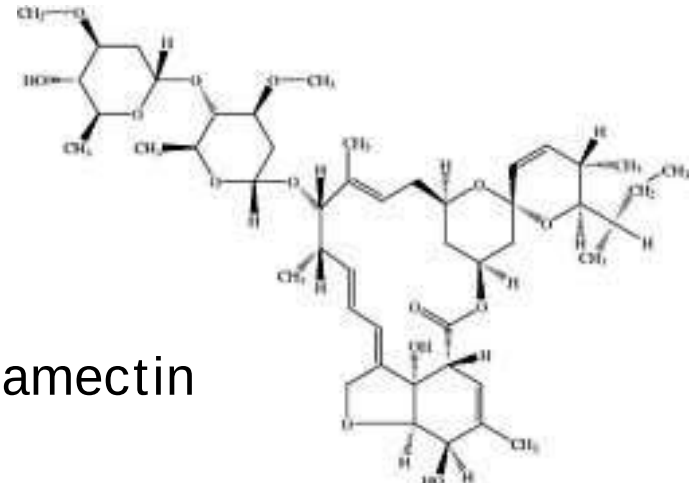
- Skin decontamination
- Supportive care
- Consider ng tube aspiration if ingested within 1 h
- Benzodiazepines for tremors or seizures
- Steroids/β-agonists as needed for allergic rxn
- Topical vitamin E oil (α-tocopherol) for cutaneous paresthesias
- Can resemble OP toxicity (bronchospasm, salivation) but atropine & pralidoxime not helpful

Other insecticides (cont'd)



- Neonicotinoids (imidacloprid, etc)
  - Partial nACh receptor agonists
    - Relatively low toxicity in humans
    - Significant toxicity only with intentional ingestion
    - Used to treat seeds (corn, soybeans)
    - Treatment is supportive care

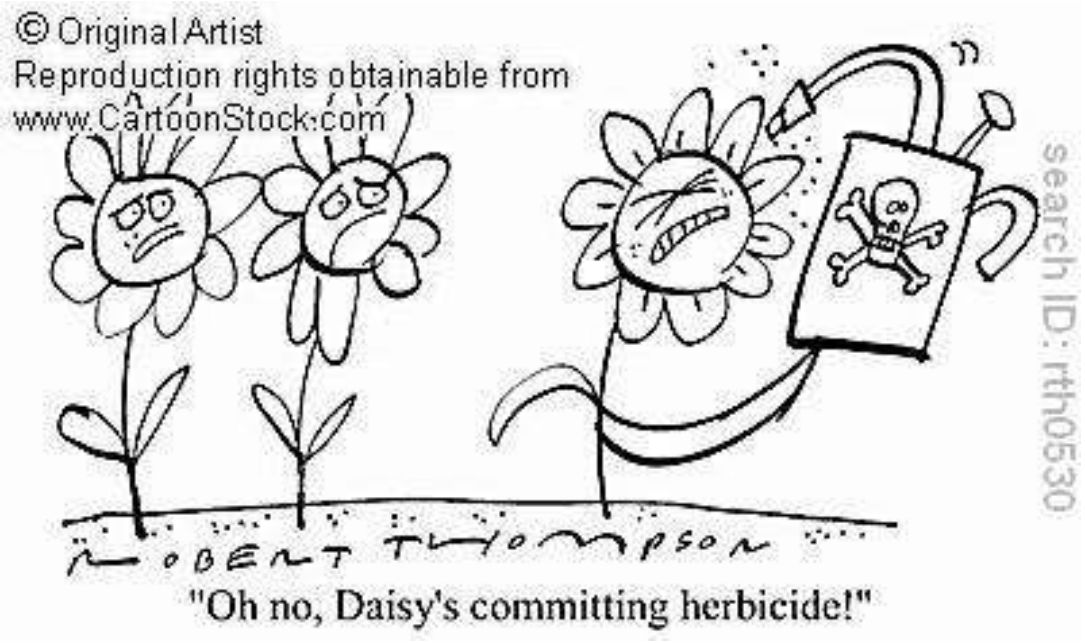
- Avermectins (abamectin, ivermectin)
  - Applied to vegetables, fruit trees, cotton, rice
  - Derived from *Streptomyces avermitilis*
  - Used for worms & ectoparsites (lice, scabies)
  - Agonist at invertebrate glutamate-gated chloride channels → paralysis in invertebrates
- Treatment: supportive care



Abamectin

Herbicides

- Chlorphenoxy herbicides
  - 2,4-D; 2,4,5-T
- Bipyridyl herbicides
  - Paraquat
  - Diquat
  - Account for most herbicide deaths
- Glyphosate
- Others
- Severe toxicity usually a/w intentional self-harm attempts
- In US agricultural sector herbicides account for ~ 80% of total pesticide use (EPA, Feb 2011)



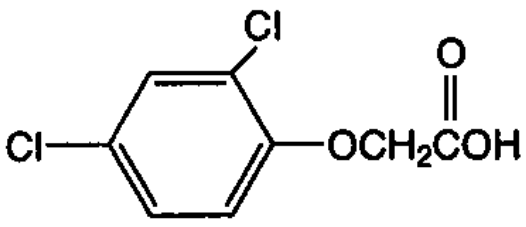
Chlorphenoxy herbicides

- Chemical analogs of auxins (a plant growth hormone) → uncontrolled and lethal growth
  - 1st herbicides - developed in 1940s
- Mechanism of human toxicity unclear
  - May interfere with energy production and neurotransmission

Agent Orange was a mixture of 2,4-D and 2,4,5-T

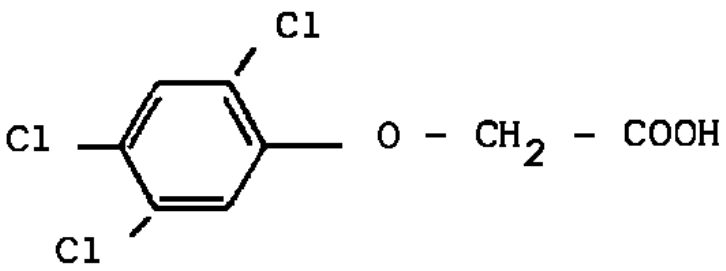
Long-term effects thought to be from contaminants (dioxins)

2,4-D



(2,4-dichlorophenoxy)acetic acid

2,4,5-T

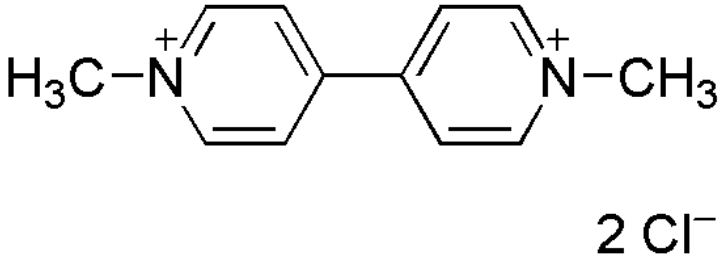


Chlorphenoxy herbicides (cont'd)

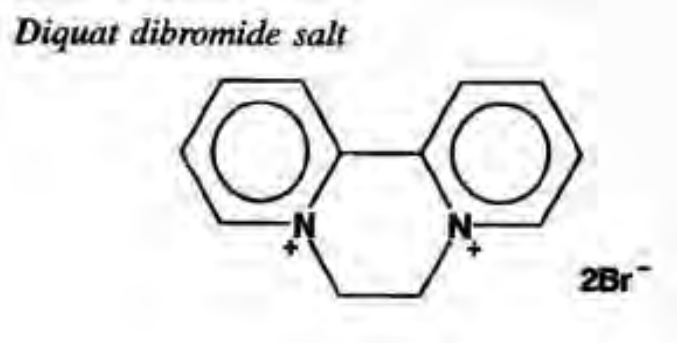
- Most poisonings are from ingestion (poor dermal absorption)
- Irritating to skin and GI tract
- N/V, QT prolongation, CNS depression, hyperreflexia with clonus, hypertonia, weakness
- Consider aspiration of ingested within 1 h
- Hemodialysis or urinary alkalinization can enhance clearance
- Supportive care

Bipyridyl Herbicides

- Paraquat/diquat
  - Highly toxic
  - Ingestion of 10-20 mL 20% solution lethal
  - Paraquat use restricted in US
- Redox cycling
  - Concentrated in lung and kidney
  - Generation of reactive oxygen species
  - Damage to membranes & other cell structures
  - Inflammatory response and fibrosis



Paraquat



Bipyridyls: Clinical features

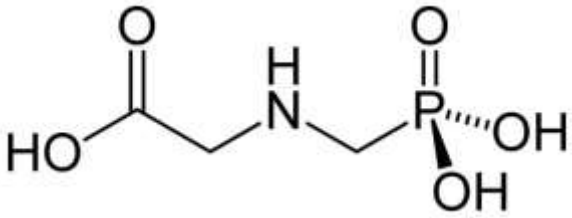
- Poor dermal absorption
  - Systemic toxicity usually from ingestion
- Sx may be delayed with dilute products
- Caustic to skin and GI mucosa
- Diquat: Severe burns to GI tract, renal failure, CNS depression, pontine hemorrhage, ARDS
- Paraquat – GI tract ulceration, renal failure, dyspnea, coma, pulmonary fibrosis
  - Qualitative urine test for screening
  - If (+) obtain serum level for prognosis

Bipyridyl herbicides: Treatment

- Skin decontamination
- GI decontamination if ingested
  - Activated charcoal or Fuller's earth
- Hemodialysis or hemoperfusion
  - Most useful within a few hours of ingestion
- Avoid O_2 unless PaO_2 <50 mm Hg
- Pain control
- Consider specific therapies
  - Immunosupression with cyclophosphamide & steroids
  - Antioxidants (Vitamin C, N-acetylcysteine)

Glyphosate

- Inhibits amino acid synthesis in plants
- Mechanism of human toxicity unclear - some likely from surfactants and other additives
  - Most common herbicide exposure reported to US poison centers
  - Major toxicity typically from ingestion
  - Issue of potential cancer risk controversial (banned in some countries)
- Symptoms
  - Skin irritation
  - N/V/D, GI caustic injury
  - Lung injury (from aspiration)
  - Acidosis, CV, renal, and CNS toxicity
- Treatment
  - Supportive care
  - Hemodialysis has been performed for severe toxicity (1)



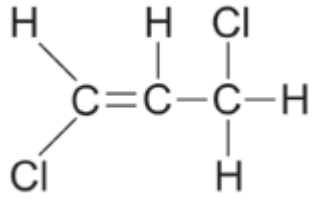
1. Garlich, *Clin Toxicol* 2011

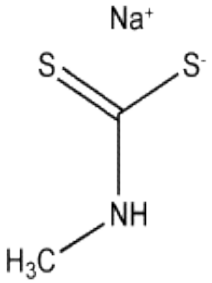
Case 2

- In Amarillo, TX a man put Al_3P pellets (obtained from a friend) under his mobile home to get rid of mice
  - Later changed his mind - tried to wash them away with water while family was at home
- Q: Why was this a bad idea?

Fumigants

- Small molecules (typically gases or volatile liquids) that diffuse rapidly
- Phosphine gas (PH_3)
  - Produced by reaction of Al or Zn phosphide with acid or water
- Methyl bromide (CH_3Br)
- Carbon tetrachloride (CCl_4)
- Dichloropropene
- Metam sodium





Fumigants: Clinical effects

- Injuries from spills or entry into fumigated structure prior to ventilation
- Mucous membrane, skin, and resp irritation; bronchospasm; delayed pulmonary edema
- Cardiac dysrhythmias
- Delayed hepatic or renal toxicity
- Neuro effects (Methyl bromide)
  - Ataxia, tremor, myoclonus, delirium

Fumigants: Treatment

- Remove from exposure
  - SCBA for rescues from confined space
- Skin decontamination
- Vomitus may off-gas PH_3 after Zn or Al phosphide ingestion
- Monitor for delayed pulmonary edema, renal and hepatic dysfunction
- Supportive care

Case 2 conclusion

- 4 children died in Amarillo, TX mobile home
  - Initially thought to be from carbon monoxide
- Father had placed Al_3P pellets under home
  - Then tried to wash away using garden hose

Washington Post 1/3/17

Strategies for poisoning prevention

- Hygienic work practices
  - Hand washing facilities or towelettes should be available
  - Facilities for rapid showering/clothing change
  - Work clothing kept out of living quarters
    - Triple washing of contaminated clothing (may be insufficient in some cases)
- Storage of pesticides in original containers
  - Storage and mixing away from living areas

Poisoning prevention (cont'd)

- Use of tractors with protective cab
- Training of pesticide workers
- Personal protective equipment
- Plasma and/or RBC cholinesterase monitoring for OP/carbamate-exposed workers
  - Baseline in advance of exposure
  - Repeat levels mid- and end of season

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