

Pesticides

lecture from Toxicology

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History

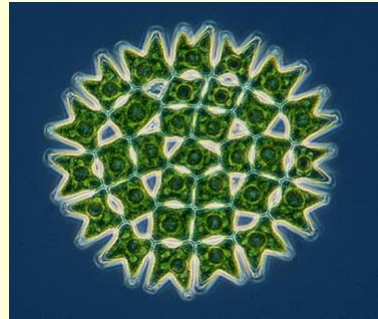
- chemicals used to kill or control pests for centuries
- the Chinese used **arsenic** to control insects
- the early Romans used **common salt** to control weeds and **sulfur** to control insects
- 1800 – **pyrethrin** was found as an insecticide
- 1920s – **petroleum oils** to control scale insects and red spider mites
- 1940s – **DDT** as an insecticide



Definitions and Terms

PESTICIDES

- used to control pests attacking food or other essential goods (leather, clothing), transmitting or causing diseases themselves
- algicides
- fumigants
- fungicides
- herbicides
- insecticides
- nematocides
- molluscicides
- acaricides
- rodenticides



Benefits vs. Risks

- **ideal pesticides** should be **selective**, destroying target organisms while leaving nontarget organisms unharmed
- **benefits** must be weighted against the **risk** to human health and environment

Benefits

- control of vector-borne diseases
- increased agricultural productivity

Risks

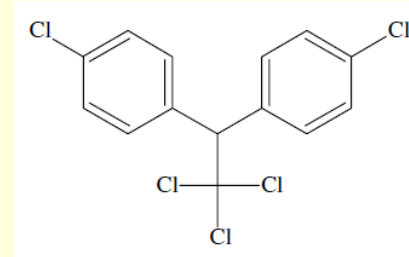
- environmental **contamination** (food chains, natural water systems)
- **persistence** in the environment, **bioaccumulation**

Organochlorine Insecticides

- introduced in the 1940s and 1950s
- DDT, methoxychlor, chlordane, aldrin, dieldrin, lindane

DDT (dichlorodiphenyltrichloroethane)

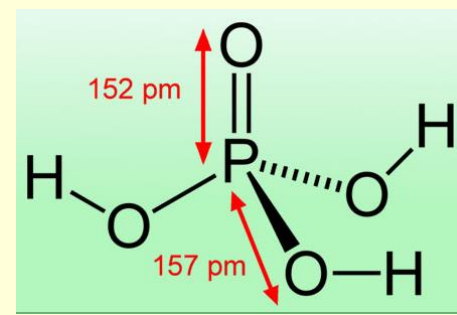
- synthesized in 1874, insecticidal properties discovered in 1939 by Dr. Mueller
- during **WWII** large quantities of DDT used to control vector-borne diseases (typhus, malaria)
- extensively used from 1940s through the 1960s in **agriculture** and **mosquito control**
- 1962 – **Rachel Carson** published **The Silent Spring** focused on the environmental impacts of DDT



DDT

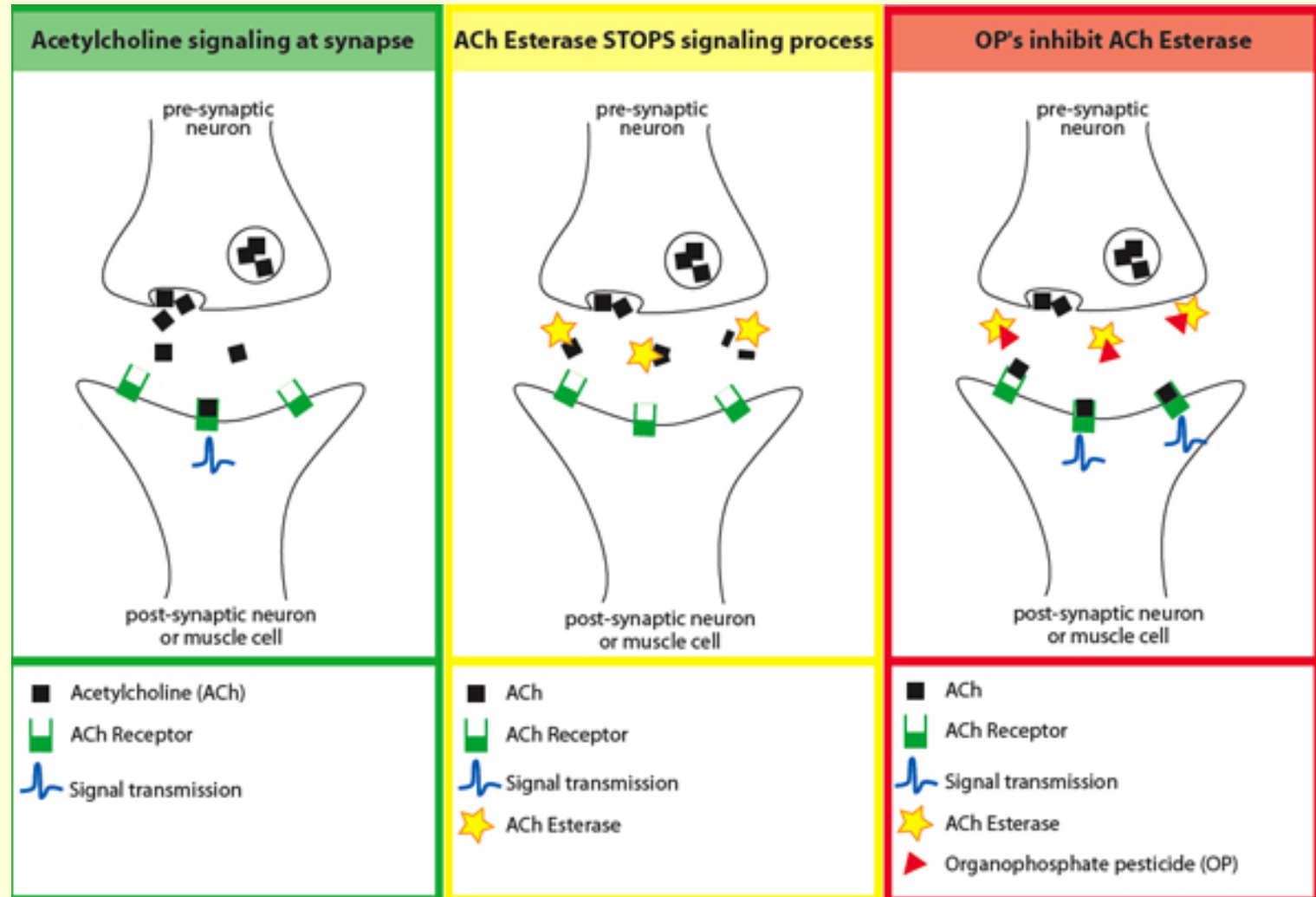
- opening Na^+ - channels in the neurons of insects causing their spontaneous firing, spasms and death
- potential mechanisms of action on humans
 - neurotoxicity
 - genotoxicity
 - endocrine disruption (antiandrogen)
 - suspected to cause cancer (liver, pancreas, breast)
- persistent, risk of bioaccumulation (plants, fatty tissue)
- DDT production and usage restricted by Stockholm Convention on Persistent Organic Pollutants (2001)
- still used under WHO guidelines against mosquitos (malaria)

Organophosphates

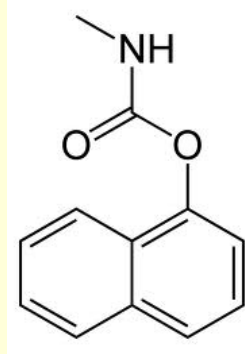


- phosphoric or thiophosphoric acid esters
- insecticides, fungicides
- **parathion, diazinon, malathion, chlorpyrifos**
- **inhibition of the acetylcholinesterase** leads to accumulation of acetylcholine and overstimulation of nicotinic and muscarinic Ach receptors
- **acute toxicity**
 - muscle weakness, dizziness, muscle cramps, paralysis, tremor
 - SLUDGEM (Salivation, Lacrimation, Urination, Defecation, GIT motility, Emesis, Miosis)
- **delayed neurotoxicity**
 - organophosphorus-induced delayed neuropathy

Organophosphates



Carbamates



- esters of N-methyl carbamic acid (H_2NCOOH)
- insecticides, fungicides, herbicides, nematocides
- similar toxic mechanisms to OP, but the AchE inhibition is more rapidly reversed, so they are less toxic

Carbaryl

- a broad-spectrum insecticide used widely in agriculture or home gardens (applied as a dust)
- not persistent, it is readily hydrolyzed
- oral LD_{50} of 250 mg/kg (rat)

Aldicarb

- application to soils on crops such as cotton, citrus, and sweet potatoes
- moves readily through soil profiles and contaminates groundwater supplies

Plant Insecticides

Nicotine

- alkaloid first used in 1763
- oral and dermal toxicity
- acute oral LD₅₀ of nicotine sulfate for rats is 83 mg/kg, dermal LD₅₀ is 285 mg/kg
- respiratory failure due to paralysis of respiratory muscles in serious poisoning cases

Neonicotinoids

- synthetic analogues of the natural insecticide nicotine
- nicotinic acetylcholine receptor agonists
- sprays, drenches, seed and soil treatments
- lead to leg tremor, rapid wing motion, paralysis and death
- imidacloprid

Plant Insecticides

Pyrethrin

- extract from several types of chrysanthemum
- nonpersistent **sodium channel modulators** lead to prolonged excitation of nerves, paralysis and death
- **low mammalian toxicity** because of rapid breakdown by liver microsomal enzymes

Pyrethroids

- **cypermethrin, empenethrin, imiprothrin**
- synthetic mimics of pyrethrins being more persistent
- greater insecticidal activity, photostability
- agricultural and urban settings, repellents
- **acute toxicity: CNS** (seizures, clouded consciousness) and **GIT** (nausea, vomiting) symptoms

New Insecticides

Fiproles

- fipronil
- used on corn, termiticide
- long-term effectiveness

Insect growth regulators

- insect juvenile hormone analogues
 - diflubenzuron
- the benzoylphenyl ureas inhibiting chitin synthesis
 - methoprene (mosquitoes, flies, fleas)
- ecdysone agonists
 - tebufenozide (catterpillars)

Herbicides

- the most widely used class of pesticides
- control and **eliminate weed** population
- new families of herbicides are developed to be relatively **nonphytotoxic to beneficial plants** and environmentally friendly

Imidazolinones

- inhibit the action of acetohydroxyacid synthase producing branched-chain amino acids in plants
- low toxicity to mammals, fish, insects and birds

Chlorophenoxy Herbicides

2,4-D and 2,4,5-T

- control of broadleaf plants by chemical similarity to the natural growth hormone **auxin**

Agent Orange

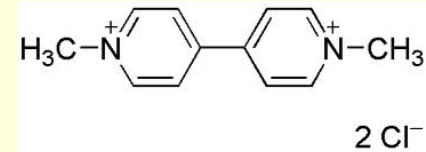
- used as a defoliant by US military during Vietnam war
- **TCDD dioxin** as a major contaminant
- toxic to developing embryos in pregnant rats
- proven carcinogen in both mice and rats (liver)
- altering the immune system



Bipyridylium Herbicides

Paraquat, Diquat

- water-soluble non-selective herbicides
- **inhibits photosynthesis** by the formation of **reactive oxygen species/radicals (ROS)**
- active against a broad range of plants, defoliant
- binds tightly to soil particles
- preferential **uptake by the lungs**
- toxicity:
 - vomiting, gastroenteritis
 - toxic nephritis with renal dysfunction and liver necrosis
 - pulmonary impairment (ARDS) and fibrosis by reactive oxygen species



Fungicides

- compounds used to **kill or inhibit fungi** or fungal **spores**
- used on variety of crops including grapes, sugar beets and ornamental plants
- **natural fungicides**
 - tea tree oil, jojoba oil, cinnamon oil, rosemary oil

Chlorothalonil

- used widely in urban environments
- relatively nontoxic



Fungicides

Dicarboximides

- captan, vinclozolin, iprodion
- inhibit triglyceride synthesis in sclerotia-forming fungi
- repeated use leads to resistance

Dithiocarbamates

- mancozeb, maneb, zineb
- used widely in urban environments
- relatively nontoxic
- do hydrolyze producing known carcinogens such as ethylthiourea (ETU)

Rodenticides

- used to **control rodents** causing losses in grain and other food storage facilities
- they harbor diseases in the form of fleas carrying bacteria and other infectious agents

Coumarins and 4-hydroxycoumarins

- **warfarin**
- anticoagulant prevent blood from clotting
- animals bleed to death in about a week
- vitamin K as an antidote

Rodenticides

Fluorides

- fluoroacetamide
 - bait pellets of grains

Thioureas

- α -naphthylthiourea (ANTU)

Alkaloids

- strychnine
- human poisonings associated with accidental or suicidal ingestion



Fumigants

- extremely toxic gases used to protect stored products (grains) and to kill soil nematodes
- applied to storage warehouses, freight car
- hazard due to inhalation exposure and rapid diffusion to pulmonary blood
- compounds requiring a license for the use



Methyl bromide

- sterilizes the soil, kill insects, nematodes, and weed seeds
- overexposure causes respiratory distress, cardiac arrest, and CNS

Chloropicrin

- highly toxic by inhalation, causes heart impairment or severe eye damage