

AGROCHEMICALS

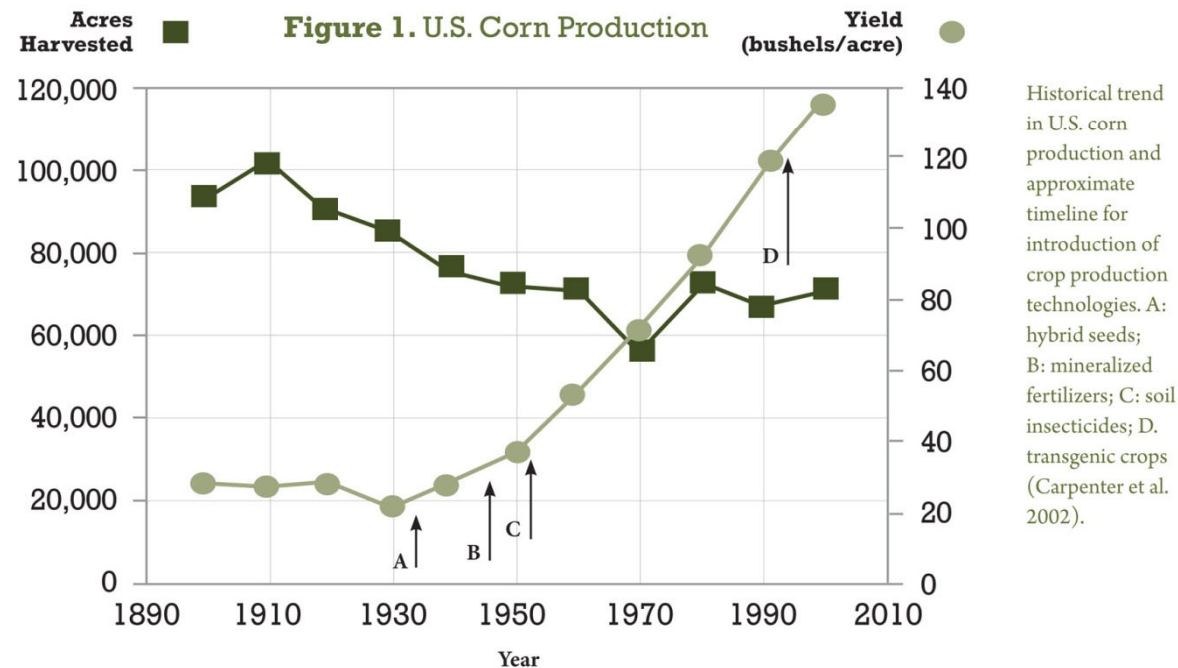
Population: 1B in 1830 to 5B in 1986 to >7B (2013)

Table 1. Percentage Use of Pesticide Classes on Major Crops During Crop Years 2003 or 2004

Crop	Herbicide	Insecticide	Fungicide
Corn	95	29	<1
Soybean	97	4	1
Wheat	45	7	2
Cotton	98	64	7
Potato	91	84	91
Apple	42	94	90

From: *Pesticides and Health: Myths and Reality*, Prof. Allan Felsot, ACSH

USDA NASS 2004, 2005

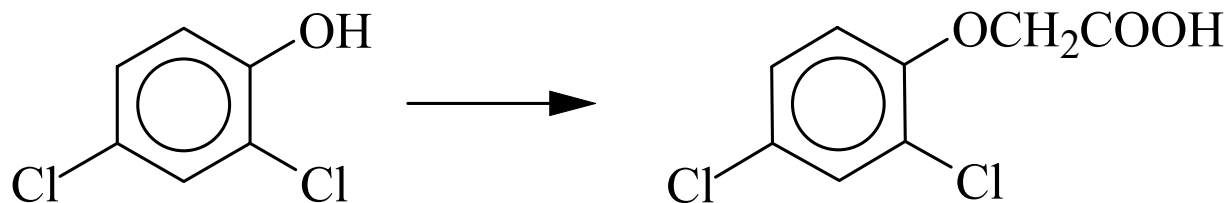


HERBICIDES (>15B\$ World, >7B\$ US alone) >0.5 B kg /y

Weeds compete for fertilizer, water,

90% corn, soya-beans, cotton, peanuts, rice treated; **75%** of herbicides go on farm crops

1946 saw introduction of 2,4-D (2,4-dichlorophenoxyacetic acid)

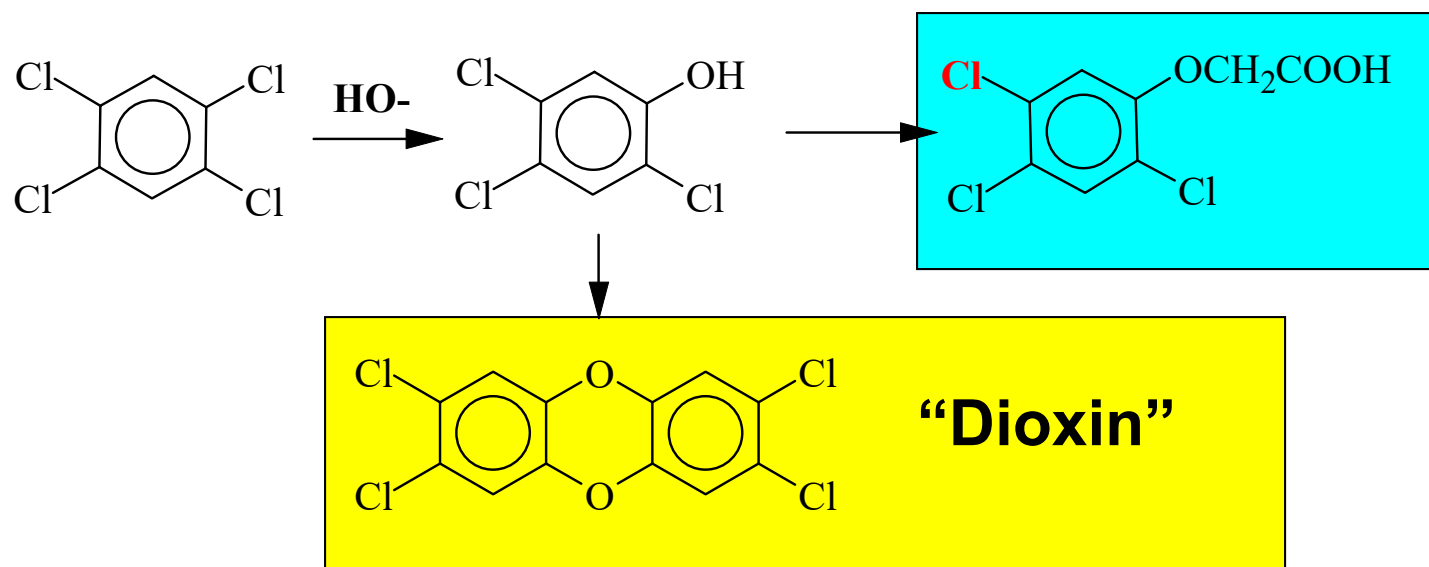


2,4-D

2,4,5-T

2,4,5-trichlorophenoxyacetic acid

which is made by a completely different process:



using tetrachlorobenzene with NaOH, **BUT is always** accompanied by some **2,3,7,8-tetrachlorodibenzodioxin**, also known as **DIOXIN**, the notorious poison

2,4-D

- kills broadleaf plants at **100g-1kg per acre**
- **cheap** (use >100M kg/yr)
- **low mammalian toxicity** ~500mg/kg orally, 1.5g/kg dermally
- **degrades** quickly in soil, does not concentrate
- can use on wheat, barley, corn, sugar, rice, GRASS (home use)

2,4,5-T

- more effective on brush, blackberries, around power lines,
- **AND THE VIETNAM JUNGLES**

**AGENT
ORANGE**



US used 70M Liters of 50:50 2,4-D/2,4,5-T in Vietnam –
AGENT ORANGE (DRUMS): sprayed neat, not diluted

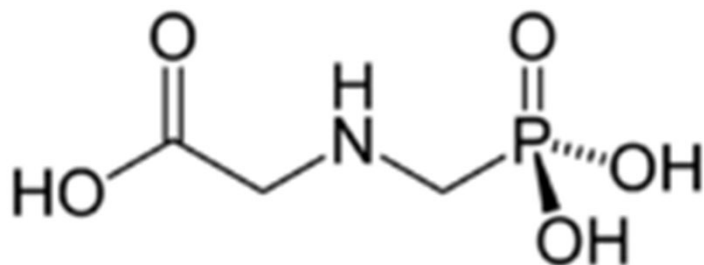
Puss, **oozing acne** and birth defects found on people sprayed -
stopped use in 1970. EPA permitted use on rice, rights of way,
home use till 1985 (later in Canada)

**Former Ukrainian
President poisoned
by dioxin in 2004**



2,4-D contains **NO** dioxin: one of safest home weed herbicides

- **imitates AUXIN**, (3-indoleacetic acid), natural growth regulator
 - causes plants to grow too rapidly
 - young cells do not mature properly, clog food transport system
-



ROUNDUP (Monsanto)
Glyphosate



- general purpose herbicide that kills **all** vegetation
- **low human toxicity**: LD₅₀ ~ 4g/kg
- Rel. environmentally benign – **deactivates in soil** quickly

Glyphosate is an enzyme inhibitor:

stops biosynthesis of the aromatic amino acids (phenylalanine, tyrosine, tryptophan) so *inhibits protein synthesis*

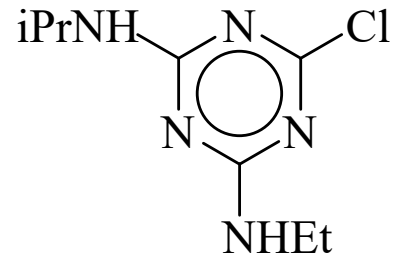
GM: Monsanto has modified corn, soybeans, canola and sugar beets; Scott has modified Kentucky Blue Grass to be Roundup Ready.

Monsanto vs. Schmeiser (1997):
Monsanto sued farmer for using GM canola but he contended the seed blew onto his fields from adjacent farms. Monsanto won but was awarded no damages.



ATRAZINE

(Ciba-Geigy, Shell, Syngenta)



Used at 1-2 kg/acre

LD₅₀ ~5g/kg

Corn is able to remove -Cl and deactivate (US: 30 Mkg/y)

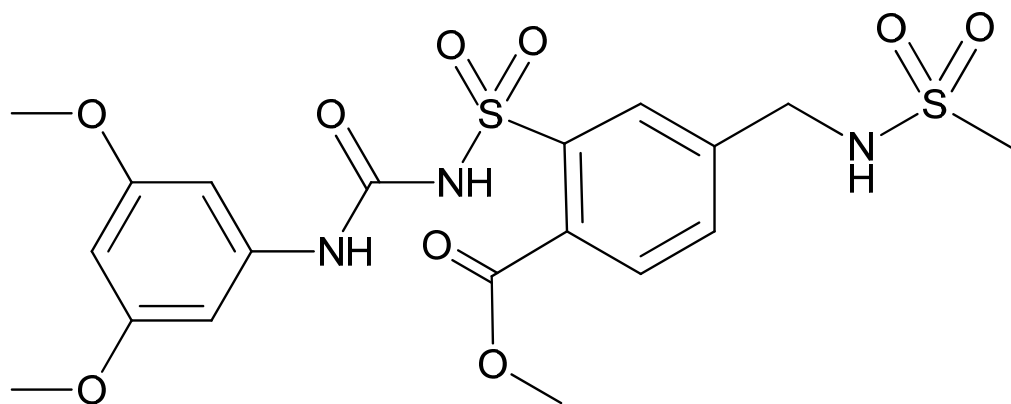
Disrupts photosynthesis: can be applied to pre-tilled land

Controversy: Banned by EU in 2004

detected in ground waters: associated the *feminization of frogs*

2001 on: SULFONYL UREAS Ar-SO₂-NH-CO-NH-Het

e.g. **Mesosulfuron-methyl** (wheat) – Bayer Crop Science



- Inhibits acetolactate synthase which synthesizes branched chain amino acids like valine, leucine
- Plants take 1-3 weeks to die



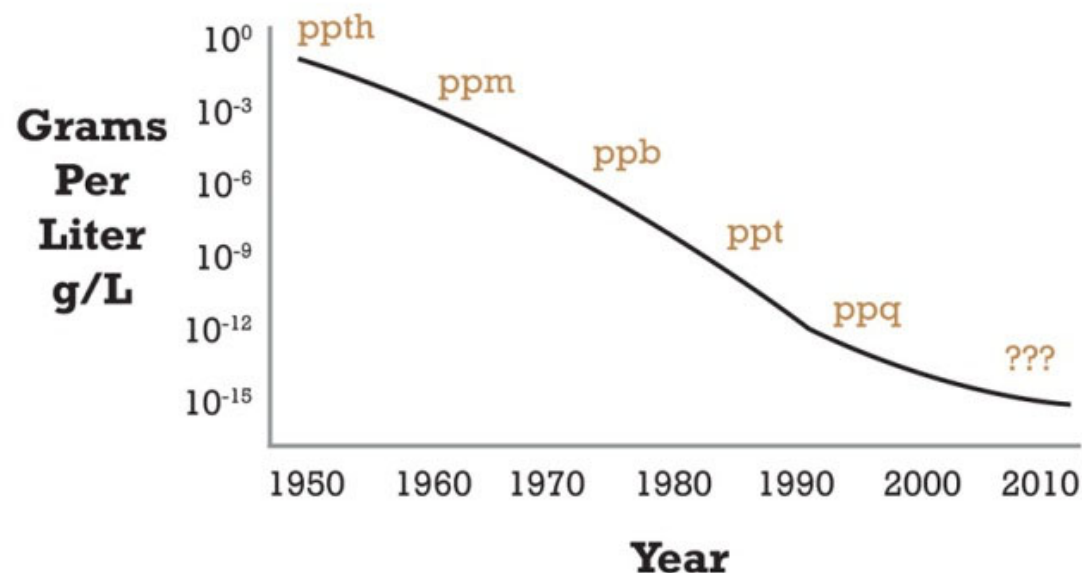
**Pesticide residues on fruit /
veggies are very small**



**Natural carcinogens, e.g. aflatoxin in
the mold on peanuts and corn is
*much more dangerous***

**Risk from carcinogens:
1/3000 motor cycle
1/300 smoking
1/25 car driving
25 x strike by lightning!!**

Figure 10. Analytical Technology Has Advanced Faster than Biological Understanding



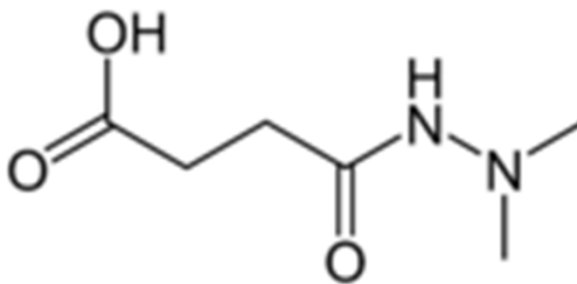
From: *Pesticides and Health: Myths and Reality*,
Prof. Allan Felsot, ACSH

Depiction of change in detection limits ($1 \text{ ppm} = 10^{-3} \text{ g/L}$) over the last 60 years of contaminant monitoring. For year 2010, uncertainty is expressed owing to the unreliability of detections reported at parts per quadrillion (ppq) and lack of articles reporting detections lower than 1 part per trillion (ppt).

Daminozide (ALAR)

Uniroyal

The great apple juice scare of '89!



- 1963-89 **ALAR sprayed on apples**: prevents bruising
- Feb '89: **'60 Minutes'** piece alleges **ALAR is a carcinogen**
- Summer 1989: Supermarkets refuse to accept ALAR-sprayed apples
- Winter '89: **FDA bans ALAR**
- 1990: Washington apple growers file suit (dismissed '94)

60 Minutes story:

<https://www.youtube.com/watch?v=7mwrWgqF4Ac>

ACSH recap in 2009

<https://www.youtube.com/watch?v=ZRO-4umbDys>

Later shown that:

- **ALAR IS a carcinogen *but...***
- **effects observed at *equiv. 20,000L juice/day and...***
- **toxins growing on bruised apples *far more potent carcinogens!***

What is the moral of this story?

INSECTICIDES

<500 BC Burning Sulfur;

1500 Arsenic

1800 Nicotine (Sulfate)

1900's Lead Arsenate

1900 Extract of dried chrysanthemum = **PYRETHRUM**

1920-1940 Japan main supplier – then war

>1940 Africa main supplier

Have to hit insect

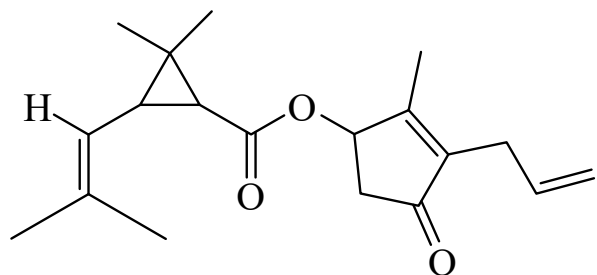
Decomposes in sunlight

(no good for crops)

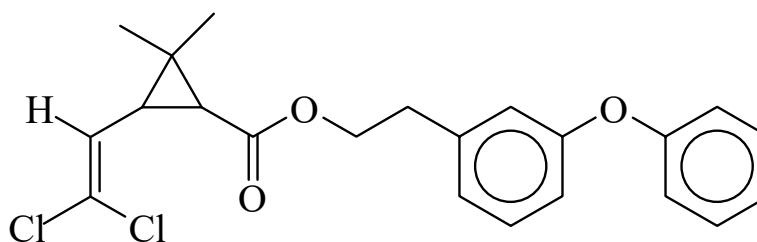
Low mammalian toxicity



By 1949 had developed more stable synthetic ones (**Pyrethroids**):



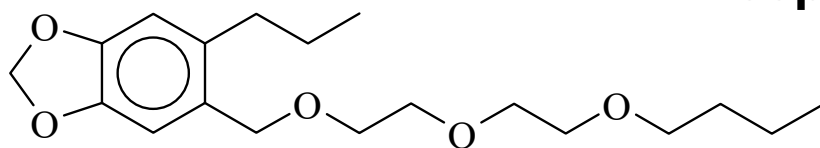
Allethrin



Permethrin

LD₅₀ = 2g/kg

Keep Na⁺ channels open: paralysis



Piperonyl butoxide



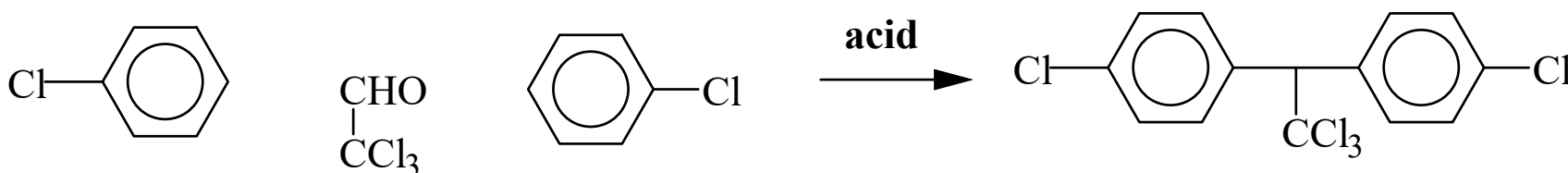
Enzyme inhibitor

Allethrin could be used in sunlight, but needs a **synergist, piperonyl butoxide**, to prevent insect recovery: **RAID**

Permethrin: cheaper, need less, more stable *ca.* 50 g/acre:
AMBUSH, POUNCE

THE CHLORINATED PESTICIDES

DDT (1873, Germany); insecticidal properties, 1939



CHEAP ca. 20 g per penny in 1940

dichloro**d**iphenyl**t**richloroethane

Wartime - pyrethrum supply cut off by Japan
Troops were lice and tick infected
Copper, Lead needed for military use

Tried DDT as 10% powder mixed with talc
directly on millions of troops
3M people treated in Naples in 1943 alone!

Mechanism: Na⁺ channels don't close, continuous nerve impulses

DDT THE GOOD

- Cheap
- Effective against all insects
- Extremely persistent
- Low toxicity to non-insects (2-3 g/kg on skin)

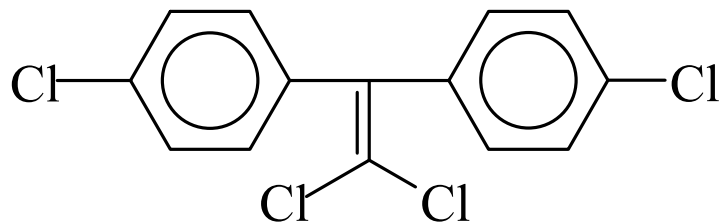
DDT THE BAD

- Cheap – indiscriminate use
- Effective against all insects – kills 'good' insects too
- Extremely persistent – around for > 20 y
- Effects on birds

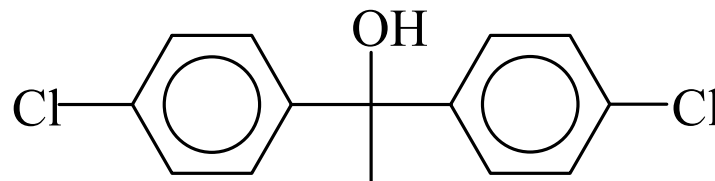
DDT – some effects:

- Crop yields went up
- Stopped Gypsy Moth in East, Spruce Budworm in West
- Reduced malaria, killed louse (Typhoid), Flea (Plague) and Tsetse Fly (Sleeping sickness)

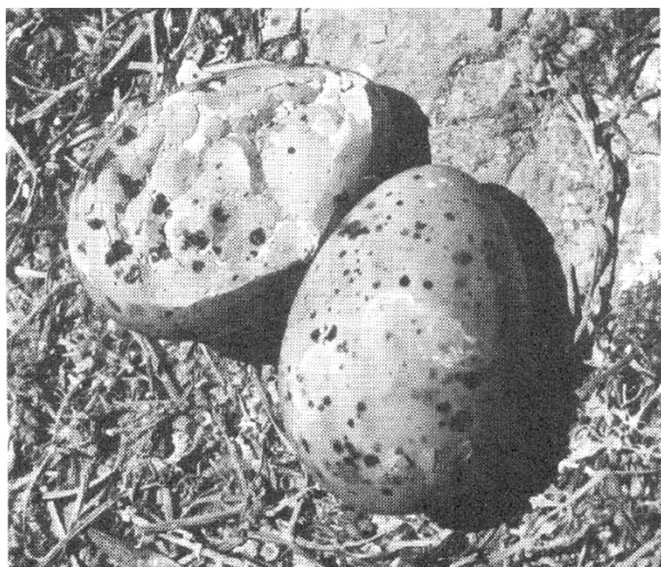
Insect Resistance - overrated!! Some insects have developed DDT-ase which dehydrochlorinates DDT to **DDE**; however that is easy to overcome by blocking the enzyme, e.g. with **chlorofenthol**



DDE



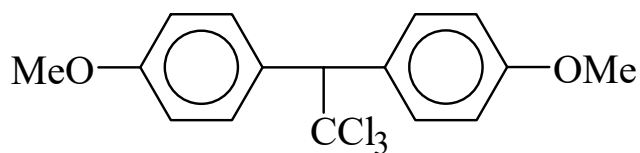
Chlorofenthol



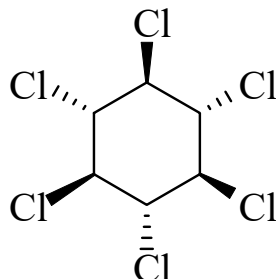
Crushed and normal eggs in a Caspian tern nest. DDT residues and consequent thinning have been related to such breakage.

Rachel Carson's Silent Spring (1962) and decline of **Bald Eagle populations** led to reduced NA usage, and eventual ban in 1972

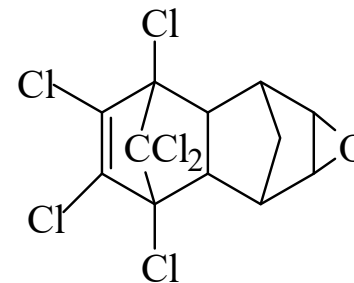
In Canada, **Methoxychlor** is widely used – degrades more quickly



Methoxychlor



Lindane



Dieldrin

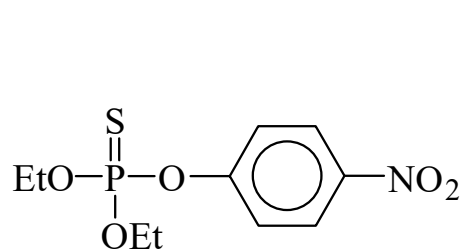
But **many** much more **toxic ones** were also made:

Lindane **LD₅₀ 100mg/kg**

Dieldrin **LD₅₀ 50 mg/kg**

toxic to fish, mammals, humans... most phased out now but residues remain buried in soils, ocean muds, lake bottoms....

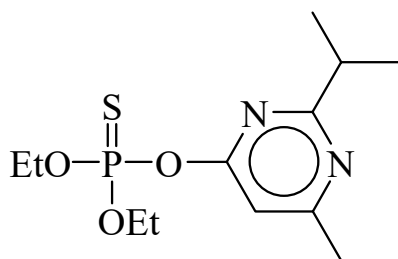
THE ORGANOPHOSPHATES - THE NERVE GASES (LIQUIDS)



Parathion

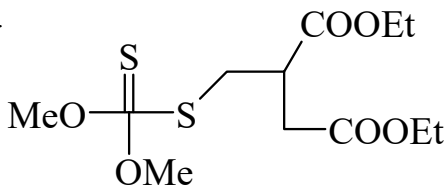
LD50

8mg/kg



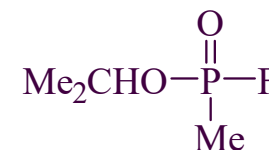
Diazinon

80mg/kg



Malathion

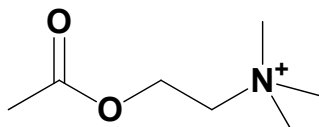
1g/kg



Sarin

0.01mg/kg (man)

Very effective – more toxic to ALL LIVING SPECIES except malathion – safest garden insecticide with methoxychlor

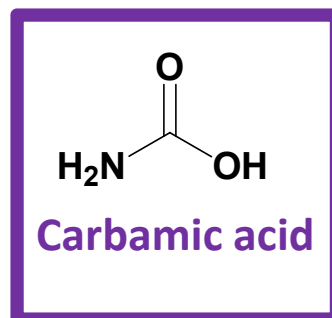
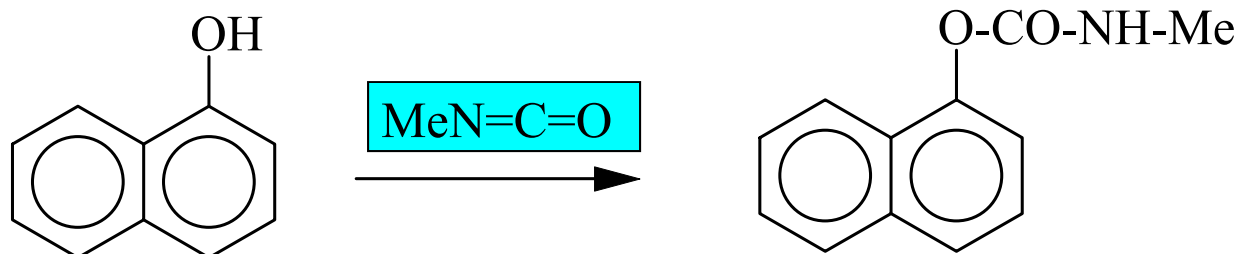


OP are **Acetylcholine esterase (ACE) inhibitors**:

- **Acetylcholine** required for **transmission of nerve impulses**
- **ACE** limits nerve impulses
- **Block ACE = continuous nerve impulses, convulsions, death**

Note: *Botulinus toxin* works the opposite way - prevents synthesis of acetylcholine - no impulses so paralysis

THE CARBAMATES: CARBARYL (SEVIN)



ACE inhibitors: *not permanent*, less toxic

Methyl isocyanate killed > 3800 people in Bhopal, India (1984) when 25-40 tons leaked from a ruptured valve in 40 mins

More than **120,000** people strongly affected (eyes, lungs) and estimates that as many as 800,000 show some effects

Union Carbide paid out >500 M\$



Figure 16.33 A male gypsy moth uses its large antennae to detect pheromones from a female.

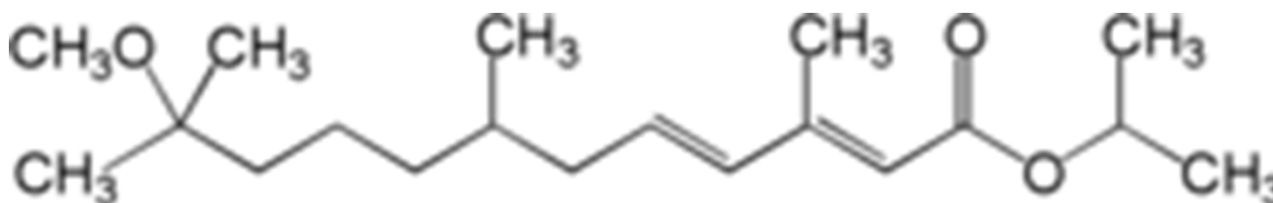
Where are we going?

Insects attract each other via
PHEROMONES: can we stop them
reproducing?

Insect Birth Control?

Or we can stop them maturing with hormones

Methoprene is approved by WHO for use in drinking water cisterns to control mosquito larvae:



keeps insect in **juvenile stage**, or with immature organs

Sandoz sell this for use in flea collars
(Precor)



Genetic modification of plants

HOW TO MAKE A GENETICALLY MODIFIED PLANT

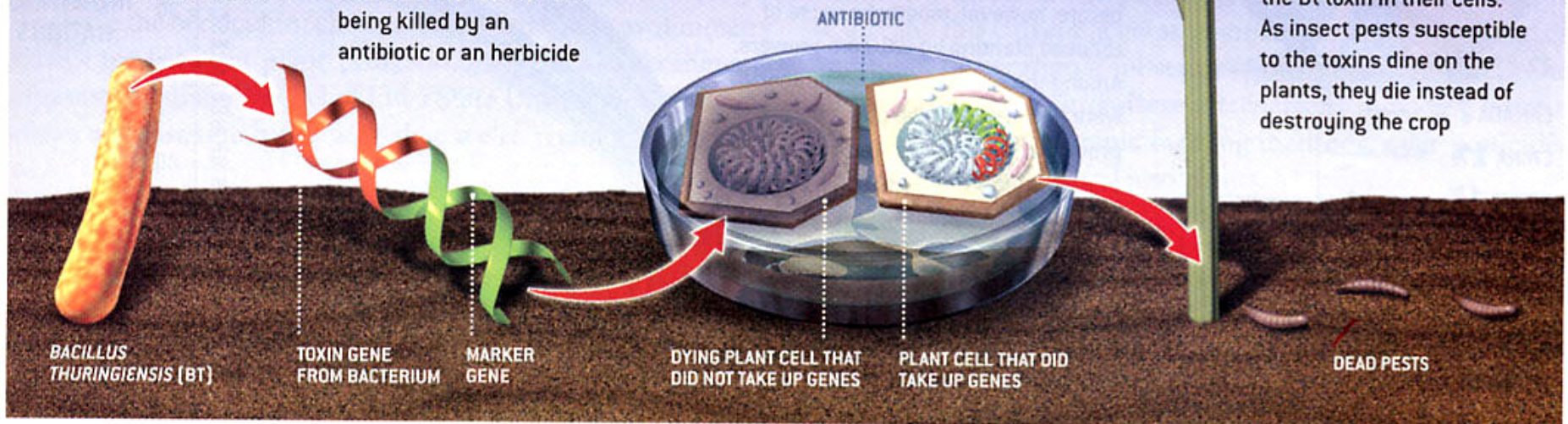
Manufacturers can produce genetically modified plants in different ways. The diagram below presents a highly simplified version of how insect-resistant corn might be made. Insect-protected GM plants are typically engineered to carry a gene from the bacterium *Bacillus thuringiensis* (Bt). This gene instructs plant cells to produce a protein that is toxic to some insects, such as caterpillars, but benign to most other creatures.

1 From the bacterium *Bacillus thuringiensis*, isolate the gene that directs cells to produce a protein toxic to certain insects

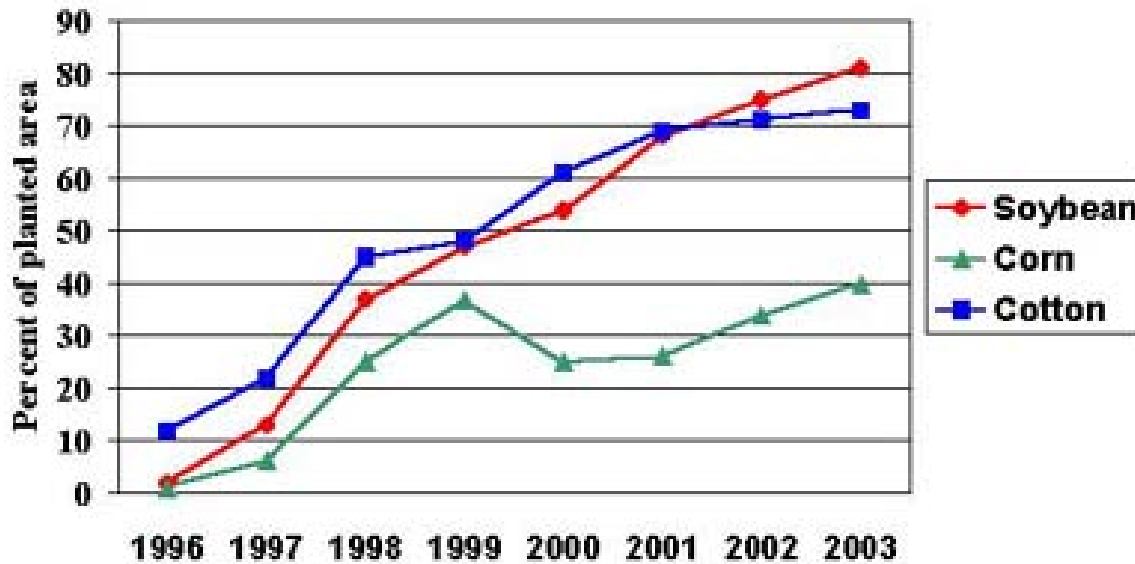
2 Try to insert into plant cells the Bt gene and a "marker" gene, able to flag cells that have taken up the Bt gene. Common markers shield cells from being killed by an antibiotic or an herbicide

3 Identify the cells that have taken up the genes, such as by exposing them to an antibiotic; only cells containing the newly inserted genes will survive the exposure

4 Allow the genetically altered cells to grow into plants. Those plants—and crops derived from their seeds—produce the Bt toxin in their cells. As insect pests susceptible to the toxins dine on the plants, they die instead of destroying the crop



U.S. adoption of genetically engineered crops (% of area planted)



Currently:

Sugar Beets

Soybeans

Corn

Cotton

Canola

New:

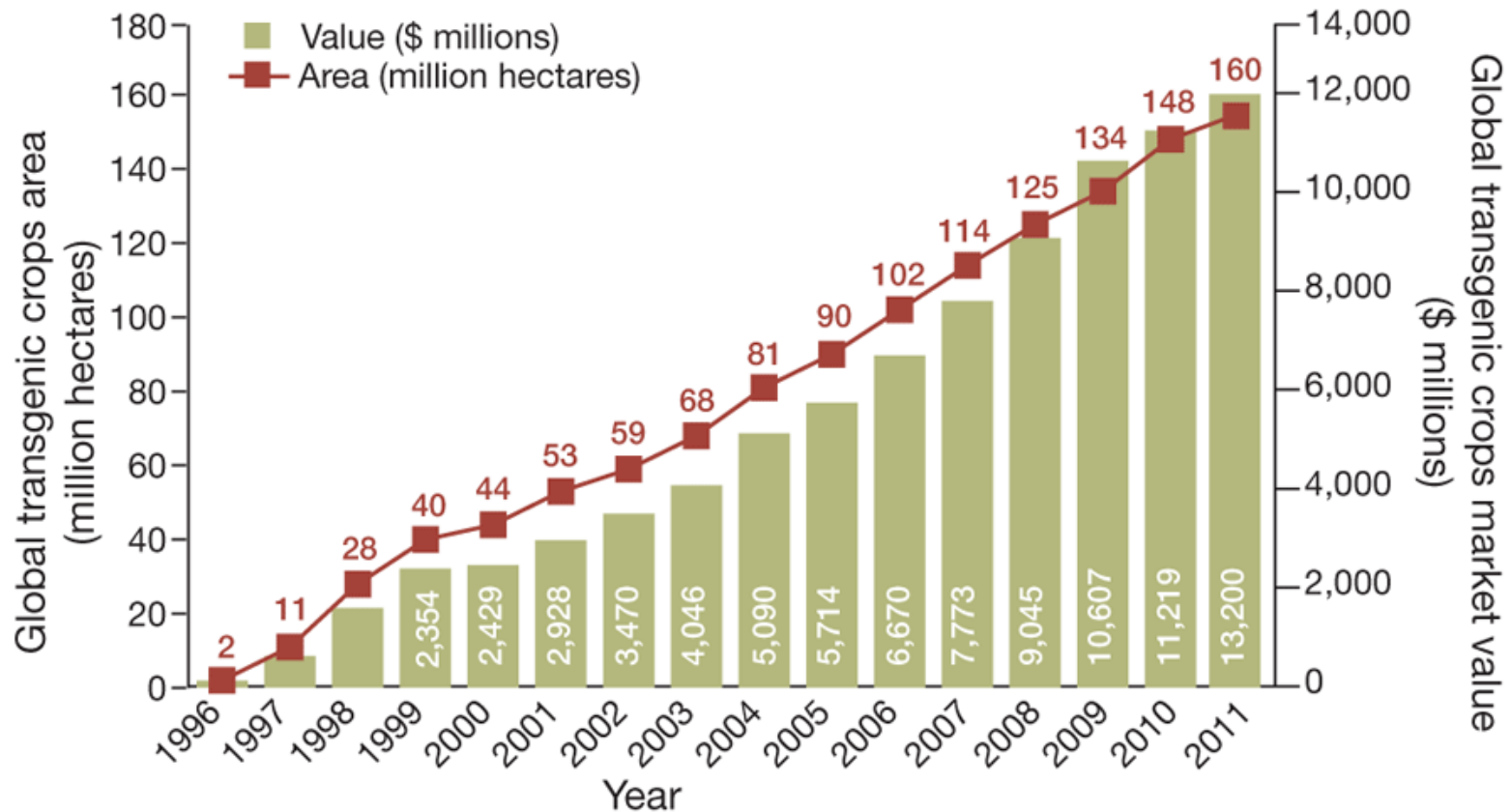
Rice

Tomatoes

with additional
vitamin A



Transgenic acreage grew 8% in 2011, now representing 36% of the global seed market.



From: A. Marshall *Nature Biotechnology* 30 (2012) 207.

Soybean and canola: mostly Round-up Ready
Cotton and corn: mostly Bt

Roundup Ready GMO's have DNA inserted from organisms that possess a version of the enzyme that is **NOT** inhibited by glyphosate.

Main issue:

Heavy reliance on Roundup is creating '*super weeds*' showing resistance to glyphosate