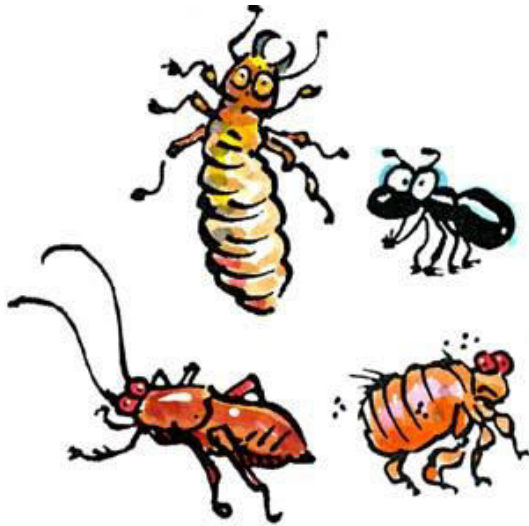


سُبْحَانَكَ اللَّهُمَّ رَبِّ السَّمَاوَاتِ السَّبْعِ وَرَبُّ الْعَرْشِ الْمَجِيدِ





# New trends in veterinary insecticides



By

Prof. Dr. Mostafa Fayez

Professor of Pharmacology

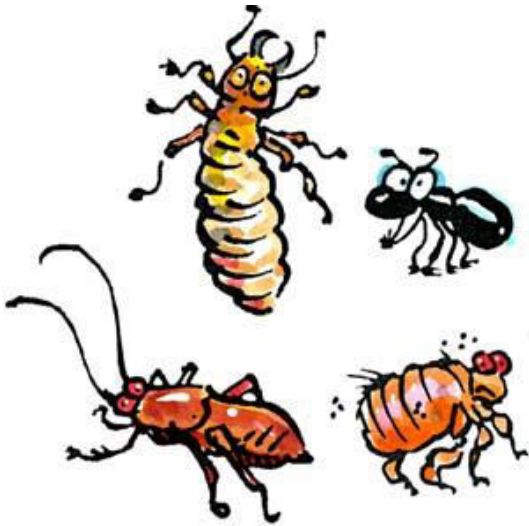
Faculty of Vet. Medicine – Suez Canal University

*Which product should I use*



# Insecticide

Any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating insects.







# IPM

Chemical

Biological

Cultural

Plant resistance

Insecticides are one of the four building blocks of IPM

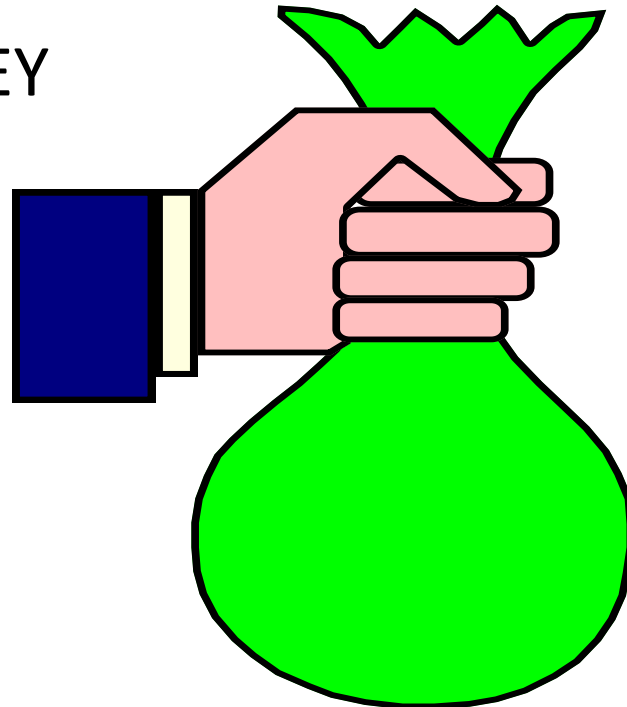


# Chemical Control: Insecticides



# We use insecticide For Only One Reason

- FOR THE MONEY

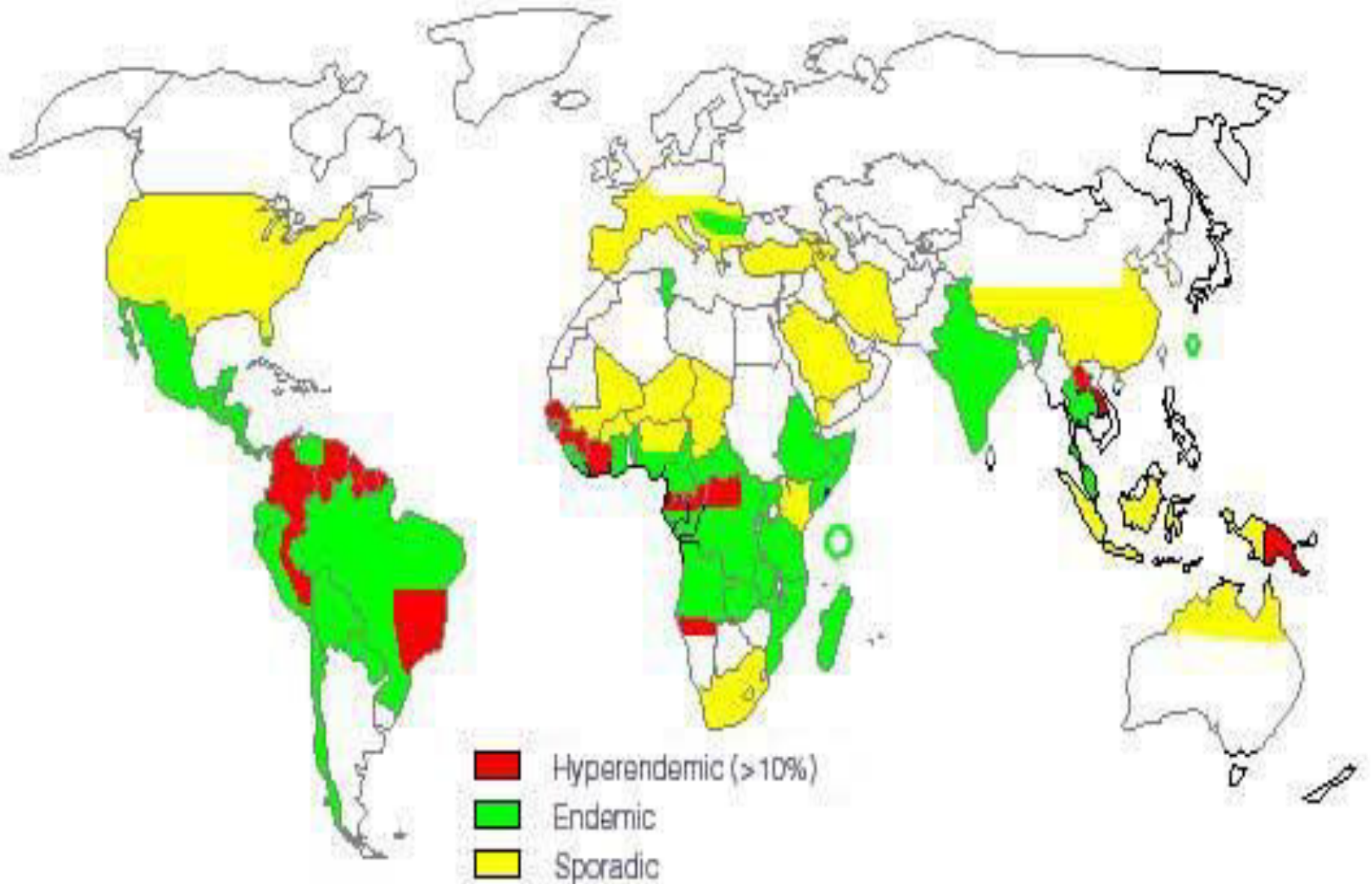




# Insecticides represent an \$ 8 billion industry



# Epidemiology



# Pesticides

## Fumigants

Phosphine

Ethylene dibromide/  
dibromochloropropane

## Fungicides

Hexachlorobenze

Pentachlorophenol

**Phthalamides**

-Captan, Folpet

**Dithiocarbamates**

-Maneb\*, Ziram

## Herbicides

**Bipyridyls**

-Paraquat\*, Diquat

**Phosphomethyl amino acids**

-Glyphosate

**Chloroacetanilides**

-Alachlor

**Chlorophenoxy Compounds**

-2,4-dichlorophenoxyacetate

## Rodenticides

Zinc Phosphide

Fluoroacetate Derivatives

$\alpha$ -naphthyl thiourea

**Anticoagulants**

-Diphacinone,  
Bromdialone

## Insecticides

### **Anticholinesterases**

-Organophosphates  
-Parathion,  
Chlorpyrifos\*  
-Carbamates  
-Aldicarb, Methomyl\*

### **Avermectins**

-Ivermectin

### **Botanicals**

-Nicotine  
-Rotenoids  
-Rotenone\*,  
Deguelin

### **Organochlorines**

-Cyclodienes  
-Dieldrin\*, Heptachlor  
-Dichlorodiphenylethanes  
-DDT\*, methoxychlor  
-Cyclohexanes  
-Lindane,  $\beta$ -HCH

### **Pyrethroids**

-Type I  
-Permethrin\*  
-Type II  
-Cypermethrin,  
Deltamethrin\*

### **Other**

-Nitromethylene  
-Chloronicotinyl  
-Phenylpyrazole

# Other pesticide terms

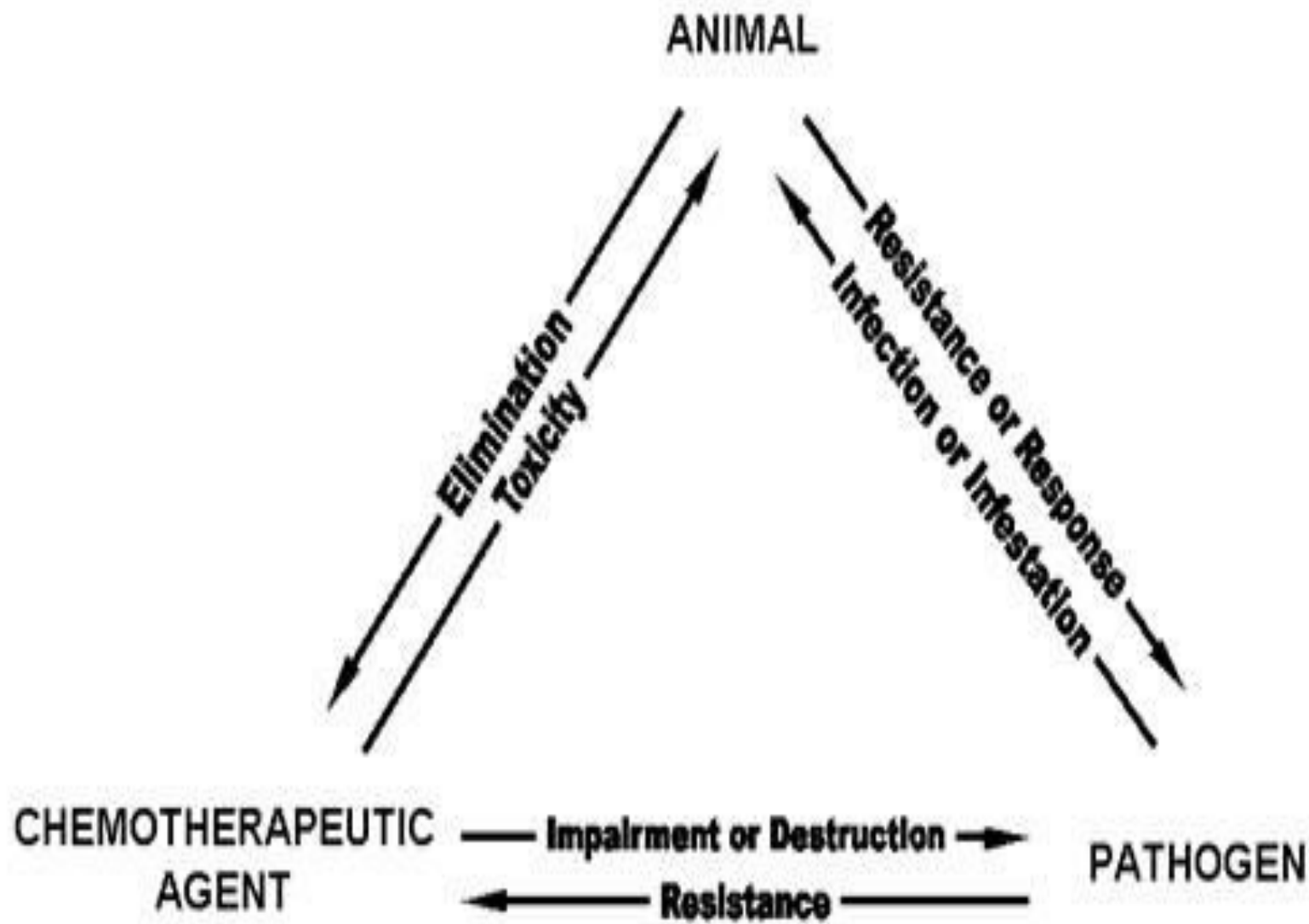
- **Ovicide -- kills eggs**
- **Larvicide -- kills larvae**
- **Adulticide -- kill adults**
- **Insect growth regulator -- disrupts normal growth and development of insects**
- **Dessicants -- cause insect death by dehydration**
- **Repellents -- repel insects and other arthropods**
- **Attractants -- attract insects and vertebrates**
- **Synergists -- chemicals used to enhance the insecticidal activity of other chemicals**

# Pesticide terms for route of entry

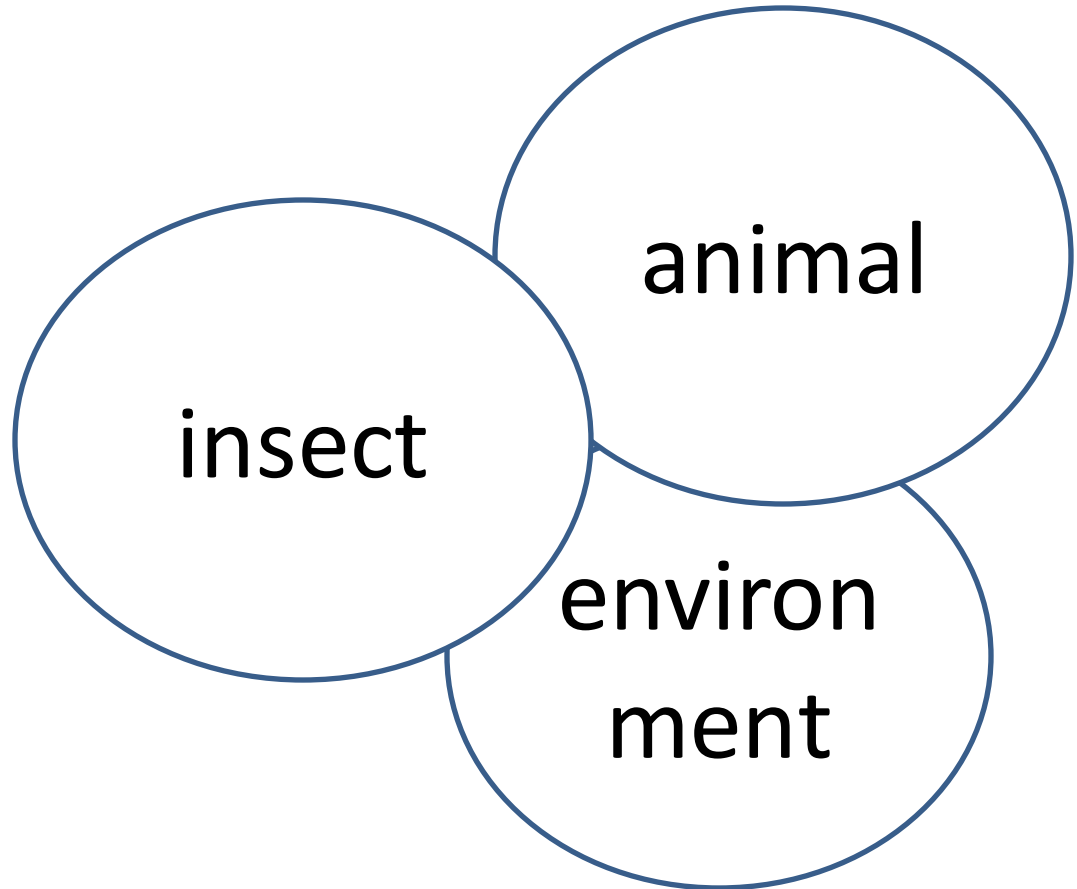
- **Stomach poison** -- enter orally usually in a food material
- Insect baits -- composed of attractive food and a toxicant
- Dusts -- applied to surfaces pests contact, pest crawls through residue, grooming results in ingestion
- Liquid baits -- boric acid and some rodenticides are water soluble and can be put in water sources of pests

# Pesticide terms for route of entry

- **Contact poisons** -- enter through cuticle of insects
  - most pesticides are contact poisons
  - most are lipophilic and enter the insect through the cuticular waxes and oils
- **Fumigants** -- vapors enter the insect through the spiracles during respiration
  - are true gases at room temperature
  - methyl bromide, sulfuryl fluoride, paradichlorobenzene, naphthalene are true fumigants



# Considerations in use of insecticides





وَعَلَّمَ آدَمَ الْأَسْمَاءَ كُلَّهَا ثُمَّ عَرَضَهُمْ

عَلَى الْمَلَائِكَةِ فَقَالَ أَنْبِئُونِي بِأَسْمَاءِ

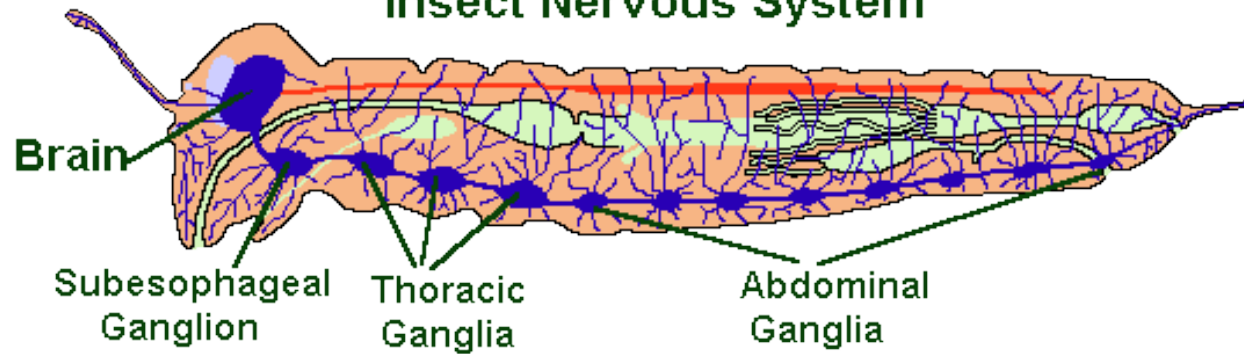
هَٰؤُلَاءِ إِنْ كُنْتُمْ صَادِقِينَ ﴿٣٦﴾ قَالُوا

سُبْحٰنَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ

أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴿٣٧﴾

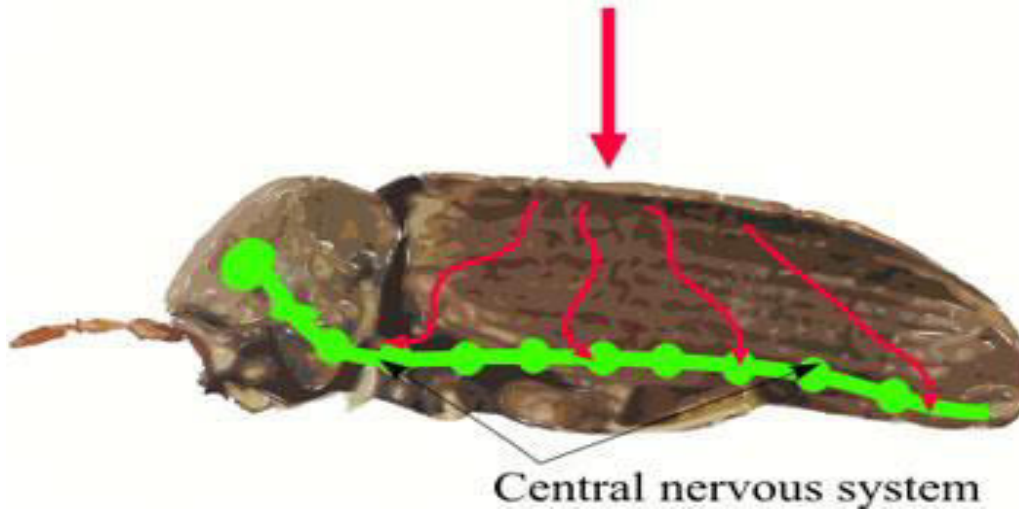
# Nervous system

A Diagrammatic Representation of the  
Insect Nervous System

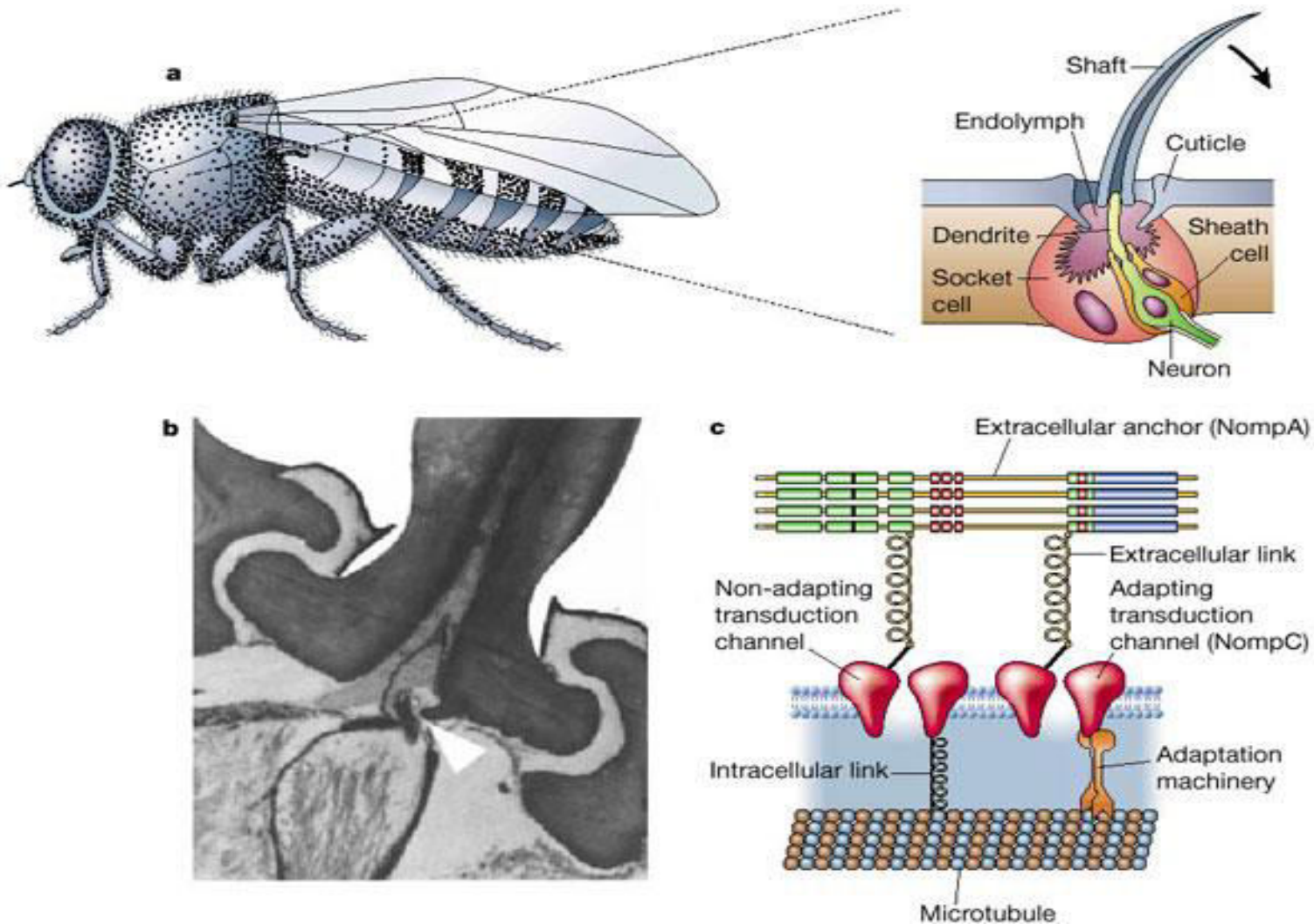


# CONTACT INSECTICIDES

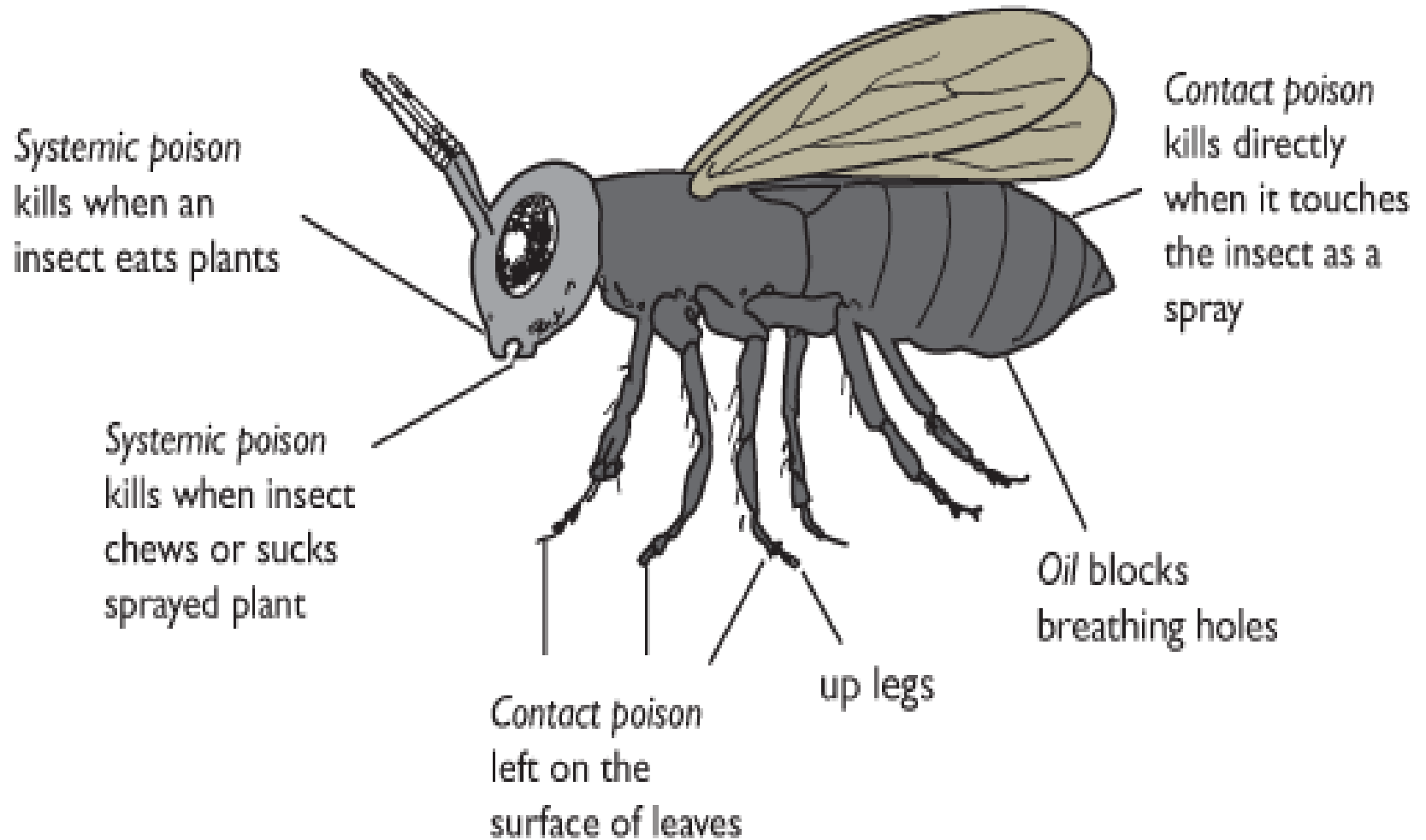
Contact insecticide



# Cuticulae



# Insects



Systemic poison  
kills when an  
insect eats plants

Systemic poison  
kills when insect  
chews or sucks  
sprayed plant

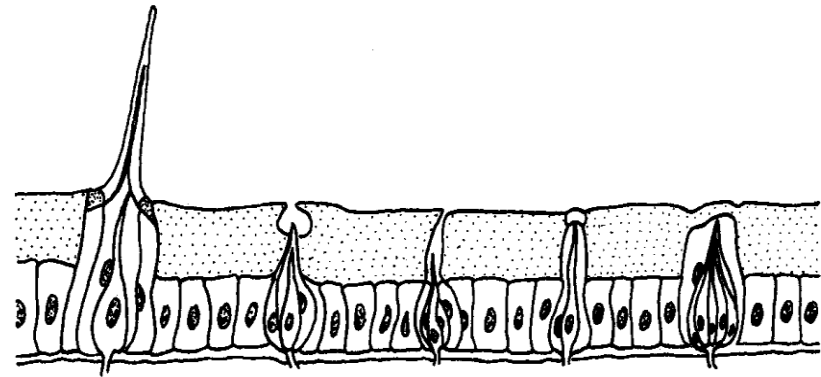
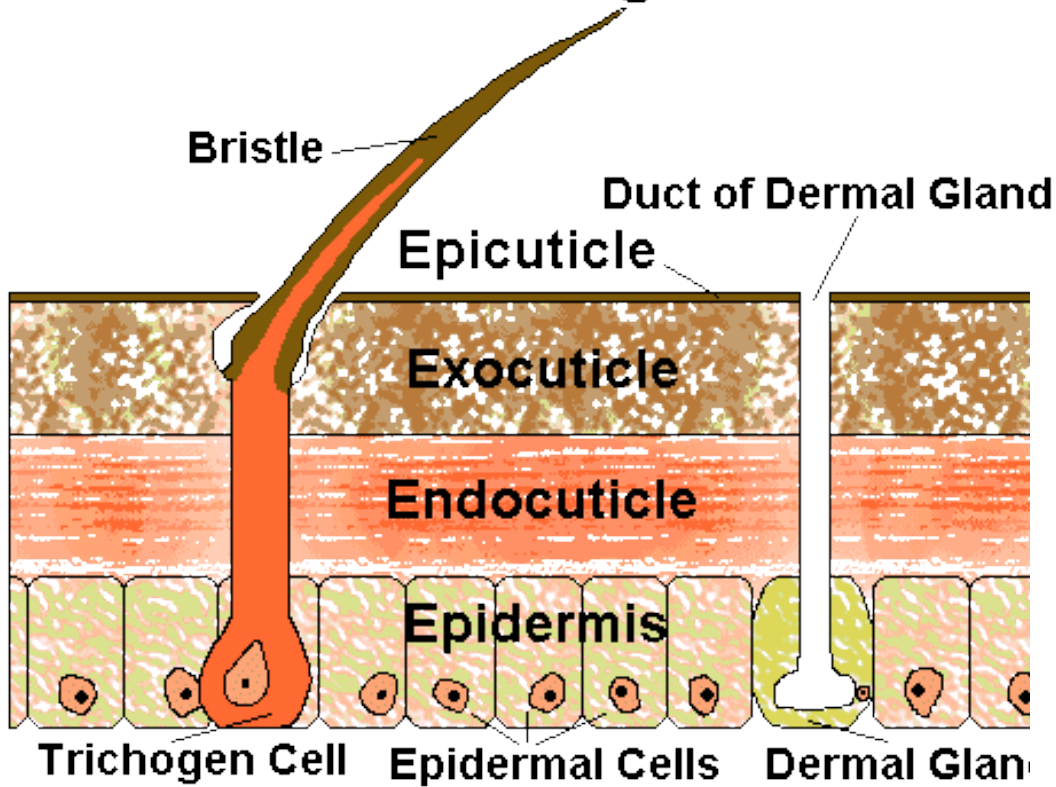
Contact poison  
kills directly  
when it touches  
the insect as a  
spray

Oil blocks  
breathing holes

Contact poison  
left on the  
surface of leaves

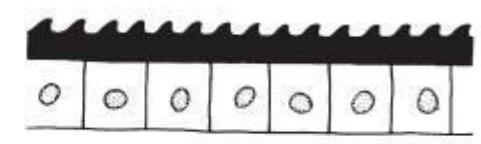
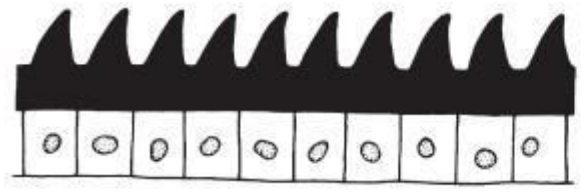
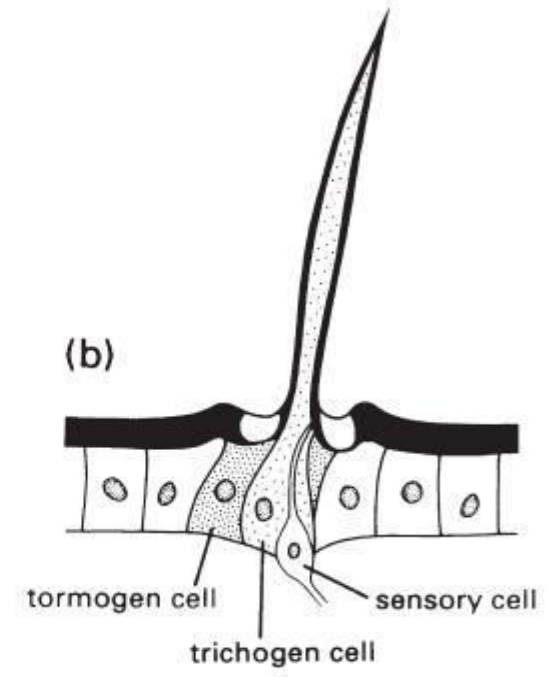
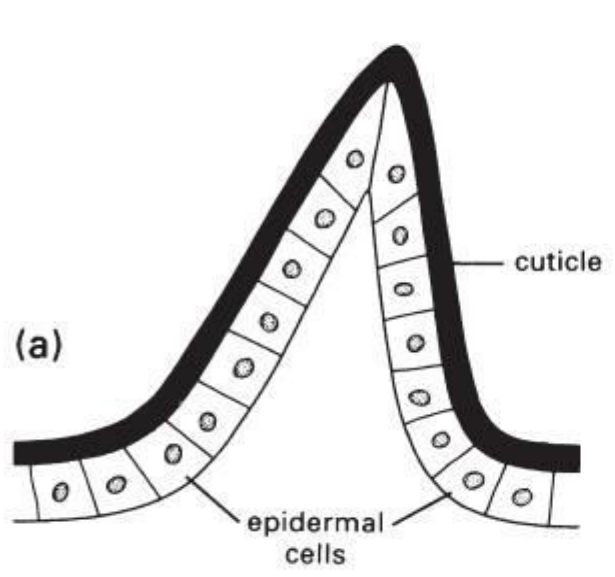
up legs

# The Insect Integument



9/4/99

# cuticle



(c)

(d)

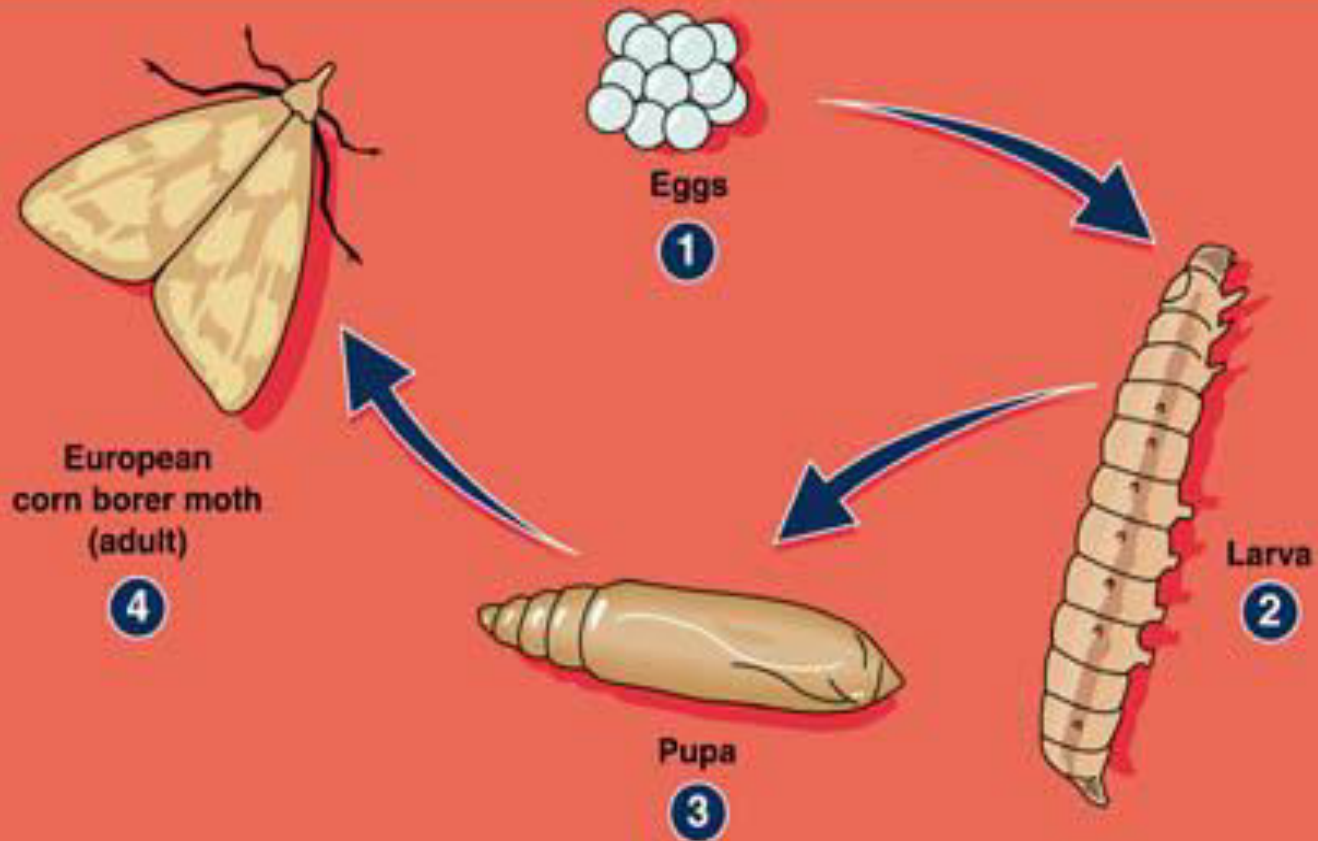






*Regal Moth* -  
adult of Hickory  
Horned Devil

# Stages of insect development

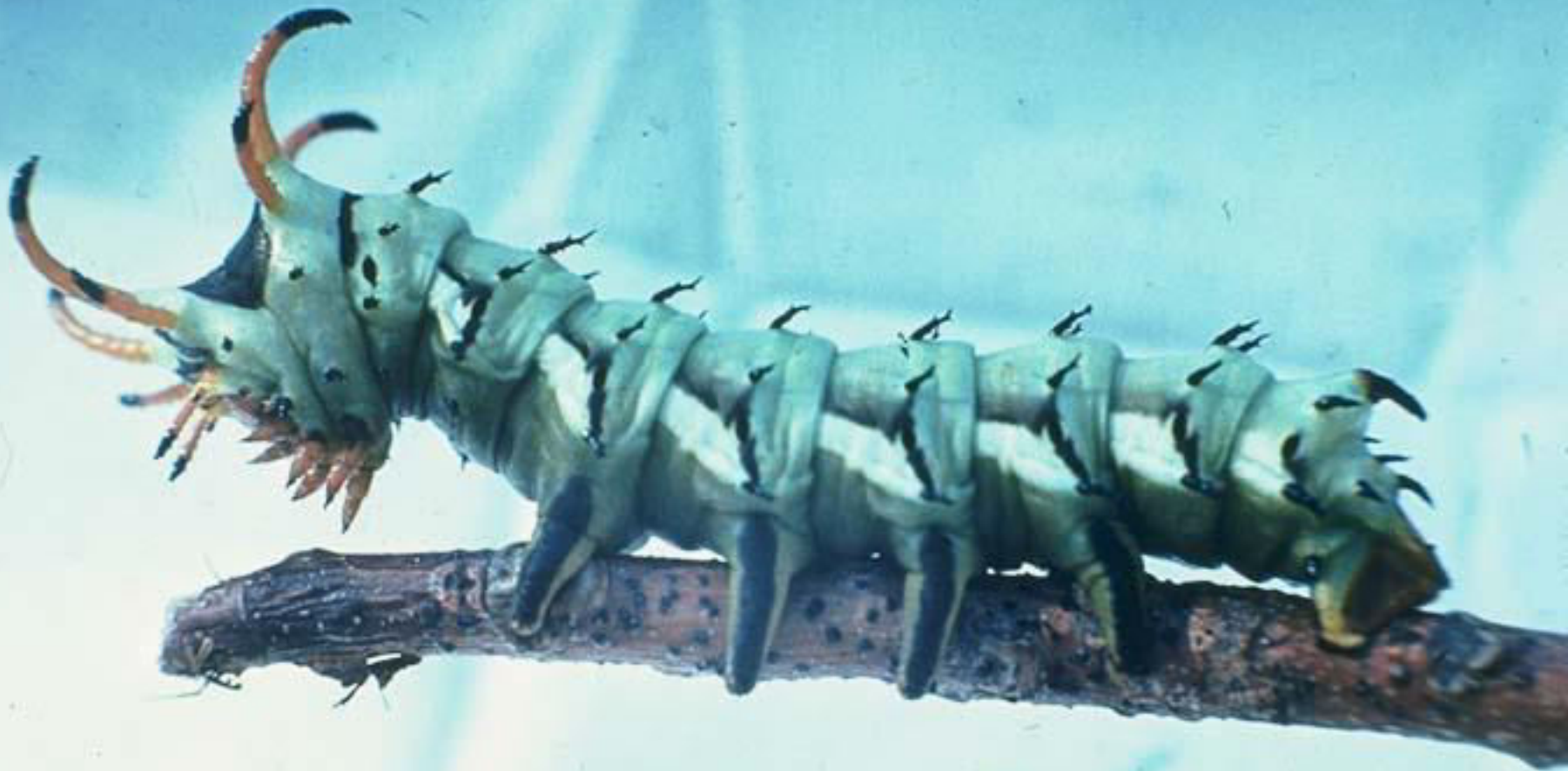


Lady bird beetle  
(ladybug)



Larva  
eating  
aphids

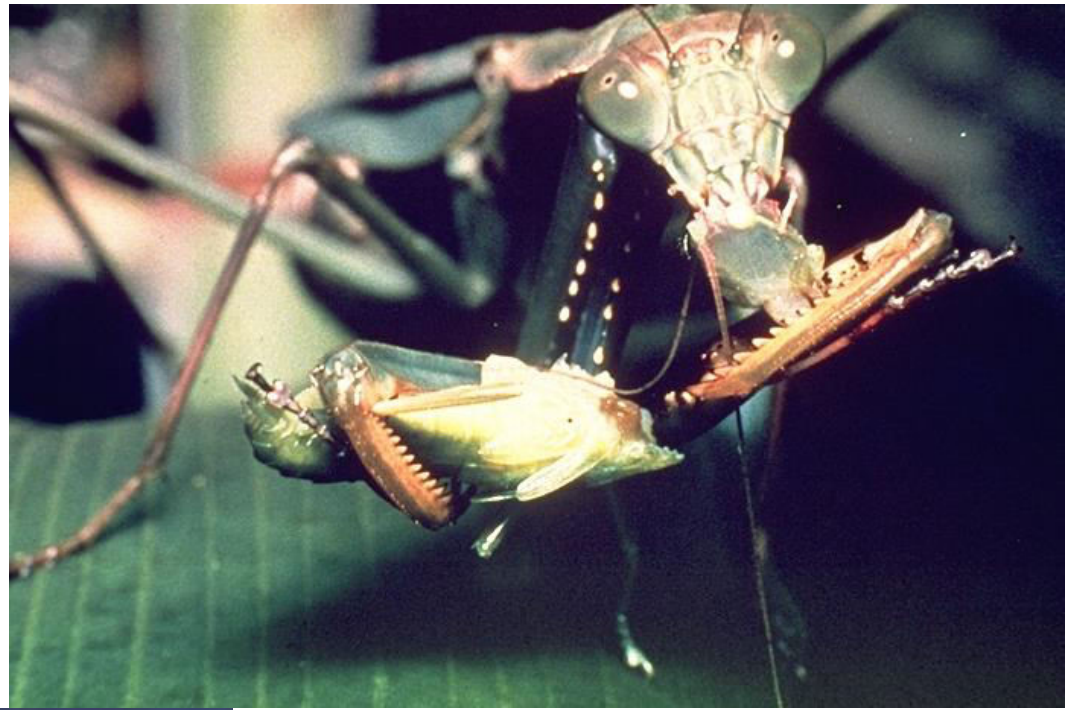
# Hickory Horned Devil





**“Hold it right there, young lady! Before you go out, you take off some of that makeup and wash off that gallon of pheromones!”**

Preying  
mantid



Lacewing  
adult





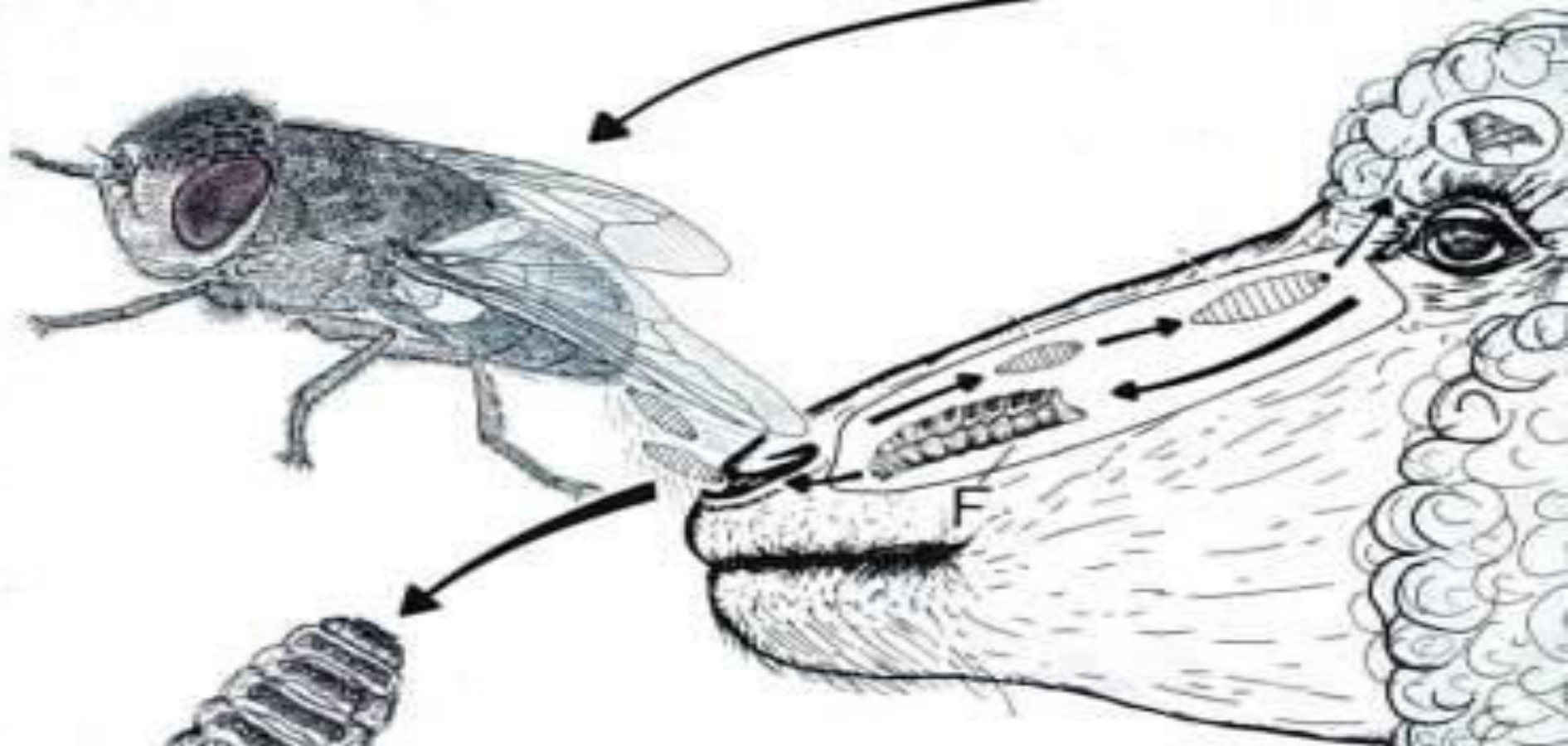














# Flystrike

Myiasis









## TAPEWORM LIFE CYCLE



**Drontal/Drontal Plus**

Biological Activity: Intestinal Disruptor

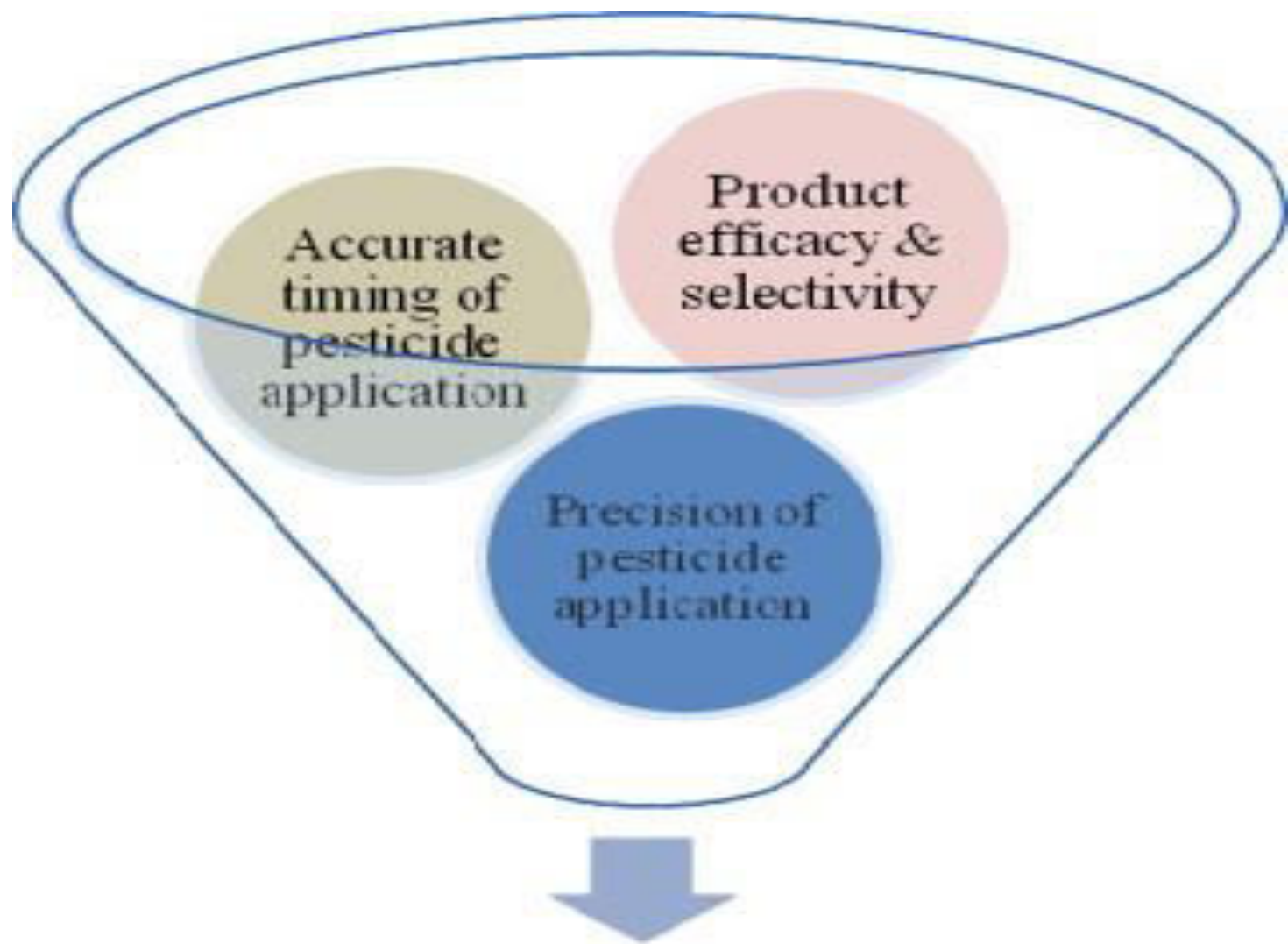
Effectiveness:  
99.9999999%



# **insecticide...??**

**“choice of insecticide”**





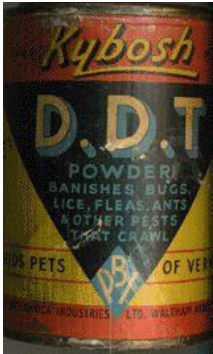
**Rational Pesticide Use (RPU)**

# Drugs used





# Examples



## Organochlorines

- DDT
- Aldrin
- Dieldrin
- Endosulfan
- Gamma HCH
- Gamma BHC

## Organophosphates

- Diazinon
- Fenitrothion
- Dichlorvos
- Dimethoate
- Malathion



## Carbamates

- Aldicarb
- Carbofuran

## Pyrethroids

- Tefluthrin
- Deltamethrin
- Lambda
- cyhalothrin
- Permethrin
- Cypermethrin



## Neonicotinoids

- imidacloprid
- nitenpyram
- acetamiprid
- thiamethoxam

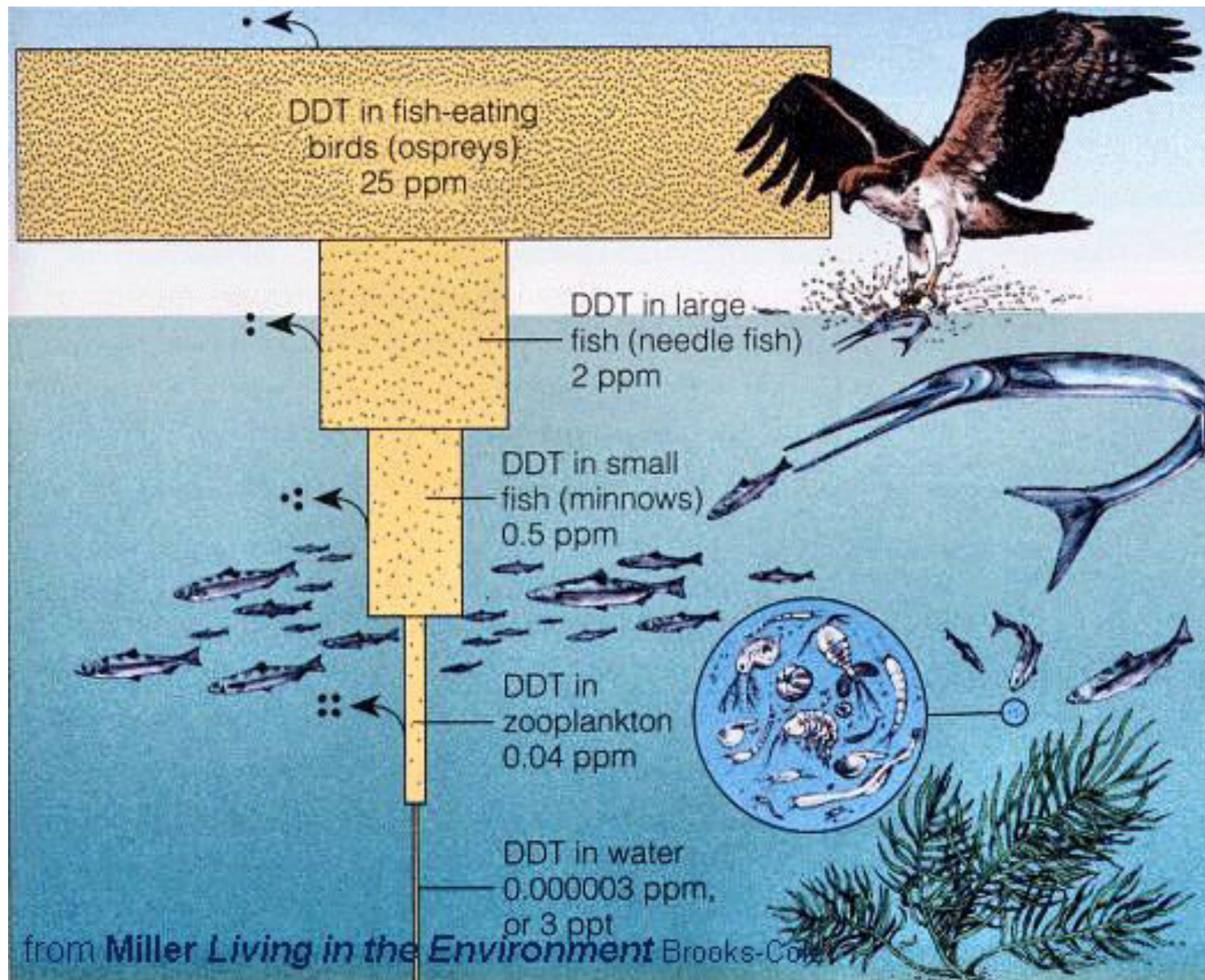


*Which product should I use*



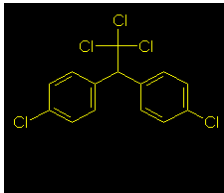




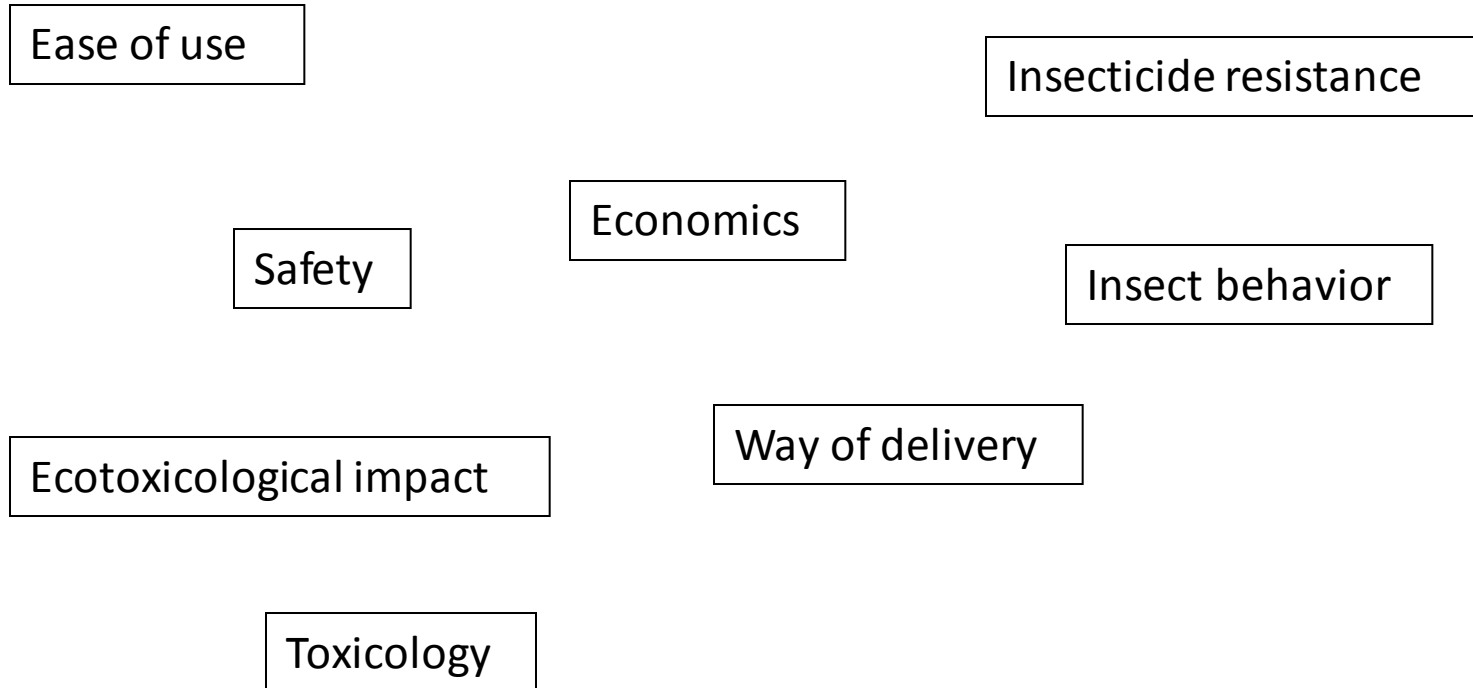


# Public concern about Insecticide use

**~100% of us have some insecticide residue in our bodies**

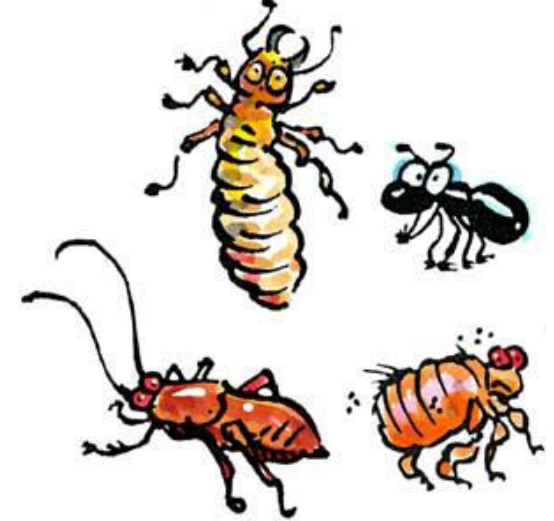


# For the Correct use of insecticides, we need to consider:



# Insecticides

- Inorganics
  - Ex. Bora-Care, Disodium Octaborate Tetrahydrate
- Botanicals
  - Ex. Pyrethrum
- Synthetic Organics
  - Ex. Pyrethroids
- “Natural”
  - Ex. Avermectins



## Insecticides

### Anticholinesterases

- Organophosphates
- Parathion, Chlorpyrifos\*
- Carbamates
- Aldicarb, Methomyl\*

### Avermectins

- Ivermectin

### Botanicals

- Nicotine
- Rotenoids
- Rotenone\*, Deguelin

### Organochlorines

- Cyclodienes
- Dieldrin\*, Heptachlor
- Dichlorodiphenylethanes
- DDT\*, methoxychlor
- Cyclohexanes
- Lindane,  $\beta$ -HCH

### Pyrethroids

- Type I
- Permethrin\*
- Type II
- Cypermethrin, Deltamethrin\*

### Other

- Nitromethylene
- Chloronicotinyl
- Phenylpyrazole

# Botanical Insecticides



## Secondary compounds

- Alkaloids
- Terpenoids
- Phenolics
- Glucosinolates
- Etc.

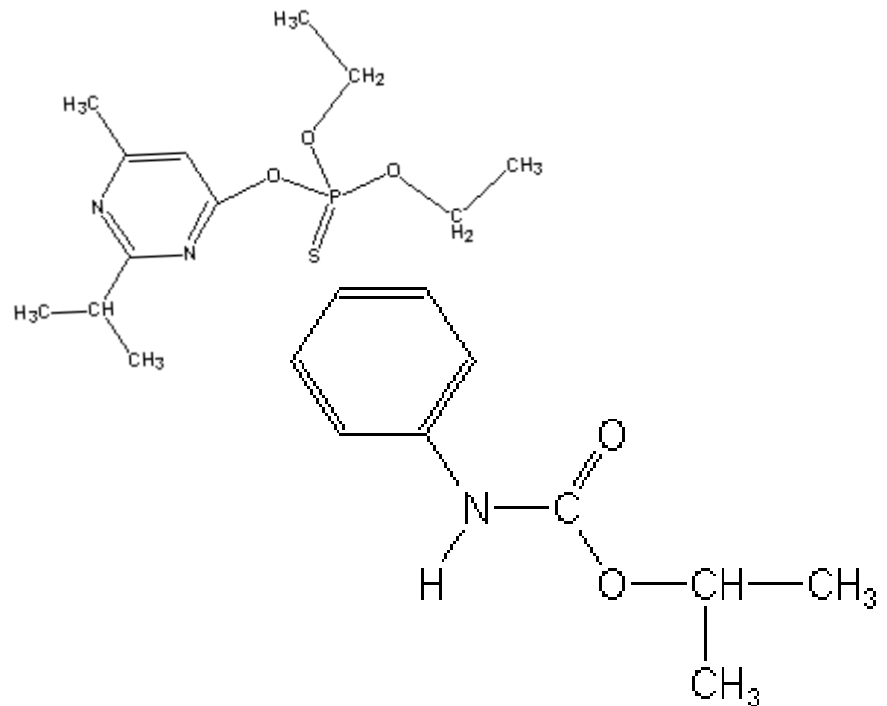
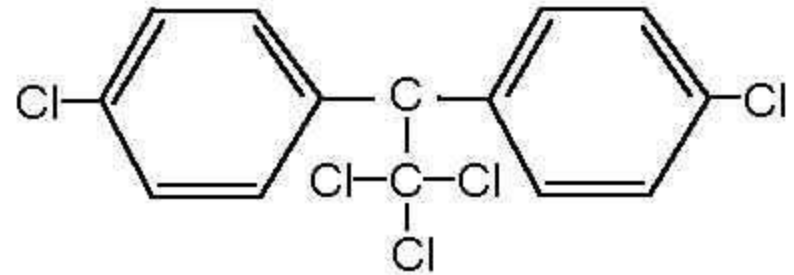
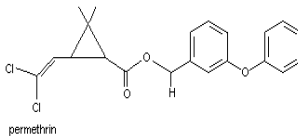
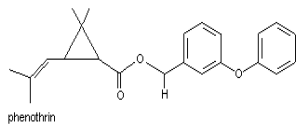




# Synthetic Insecticides

## Synthetic Insecticides

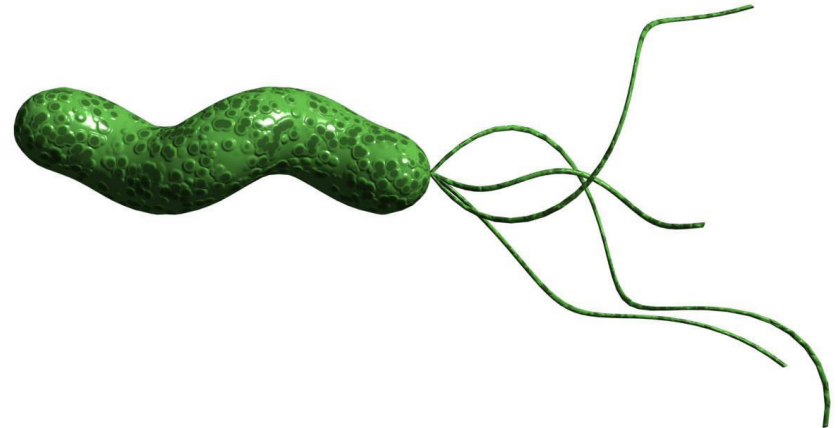
- Organochlorines
- Organophosphates
- Carbamates
- Pyrethroids
- Neonicotinoids



# Biorational Formulations

## Biorational Formulations

- Growth regulators
- Pheromones
- Microbial formulations

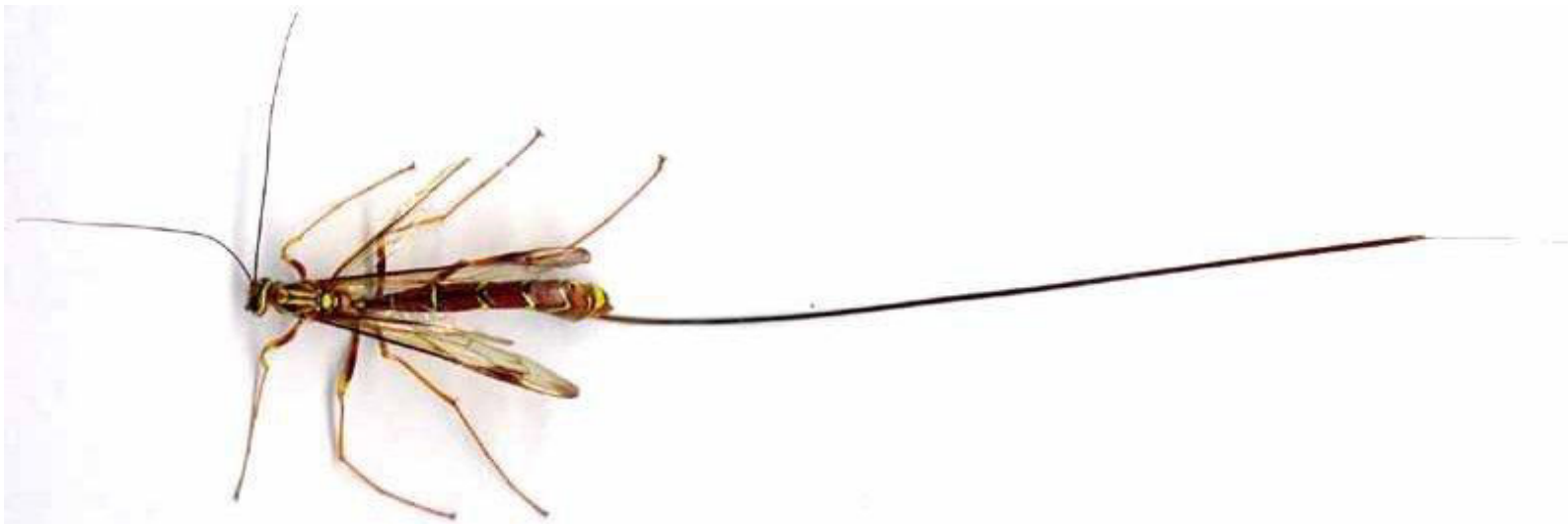
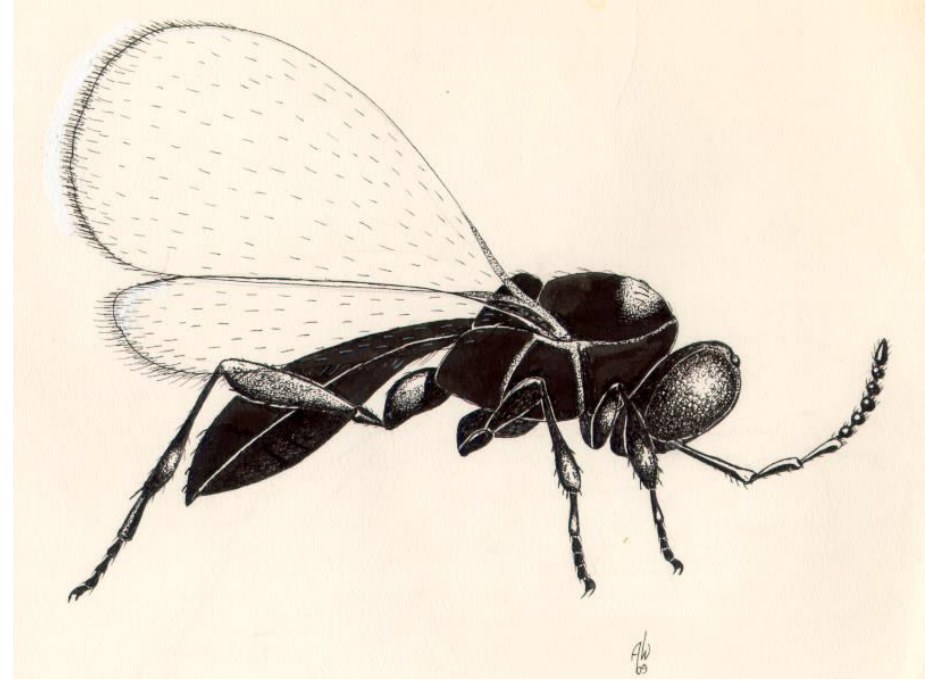


# Microbial Formulations

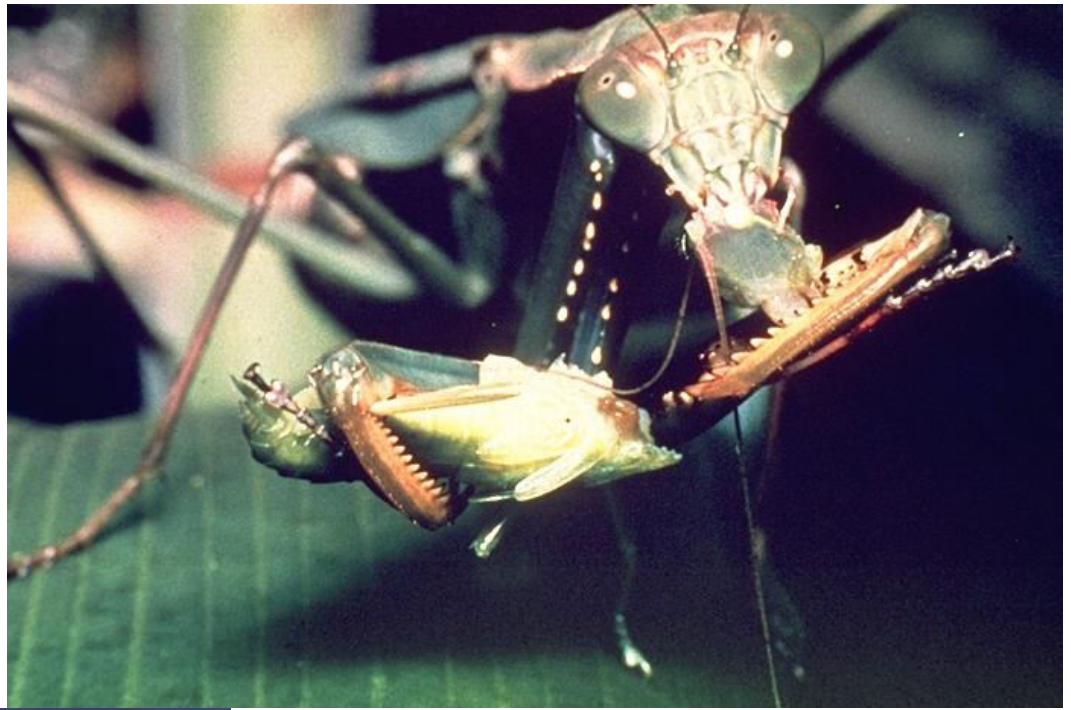
- Uses bacteria, fungi, nematodes, protozoa and viruses
- Mostly used as inundative releases
- Specific for arthropods

# Parasitoids –

- Chalcid wasps
- Cynipid wasps
- Ichneumonid wasps
- Numerous Diptera



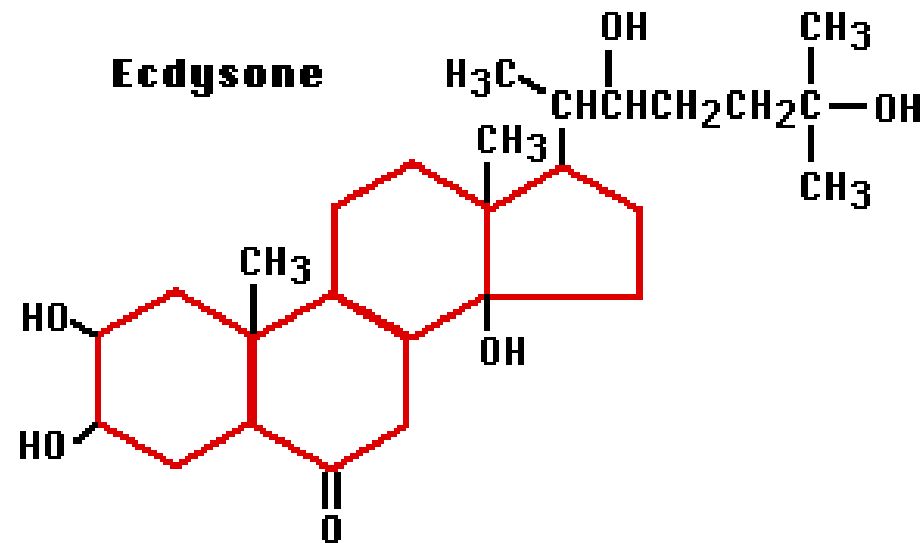
Preying  
mantid



Lacewing  
adult

# Growth Regulators

- Interfere with development
- Disrupt metamorphosis and reproduction
- Specific for arthropods





© Edith Smith 2009  
[www.butterfliesetc.com](http://www.butterfliesetc.com)

# Pheromones

- Mediate intraspecific interactions
- Around 50 available for IPM
- Mostly use in association with traps





# Classes of Insecticides



## Botanical Insecticides

- Sabadilla
- Nicotine
- Quassia
- Unsaturated isobutylamides
- Ryanodine
- Naphtoquinones
- Rotenone
- Sweet flag
- Marigolds
- Pyrethrum
- Azadirachtin
- Essential oils
- Botanical insecticides

## Synthetic Insecticides

- Organochlorines
- Organophosphates
- Carbamates
- Pyrethroids
- Neonicotinoids

## Biorational Formulations

- Growth regulators
- Pheromones
- Microbial formulations

# Examples

## Juvenile Hormones

- Methoprene
- Tebufenozide
- Fenoxycarb
- Pyriproxifen

## Chitin Synthesis Inhibitors

- Diflubenzuron
- Hexaflumuron
- Triflumuron

## Triazine Derivatives

- Melamine
- Cryomazine



# World Health Organization (WHO)

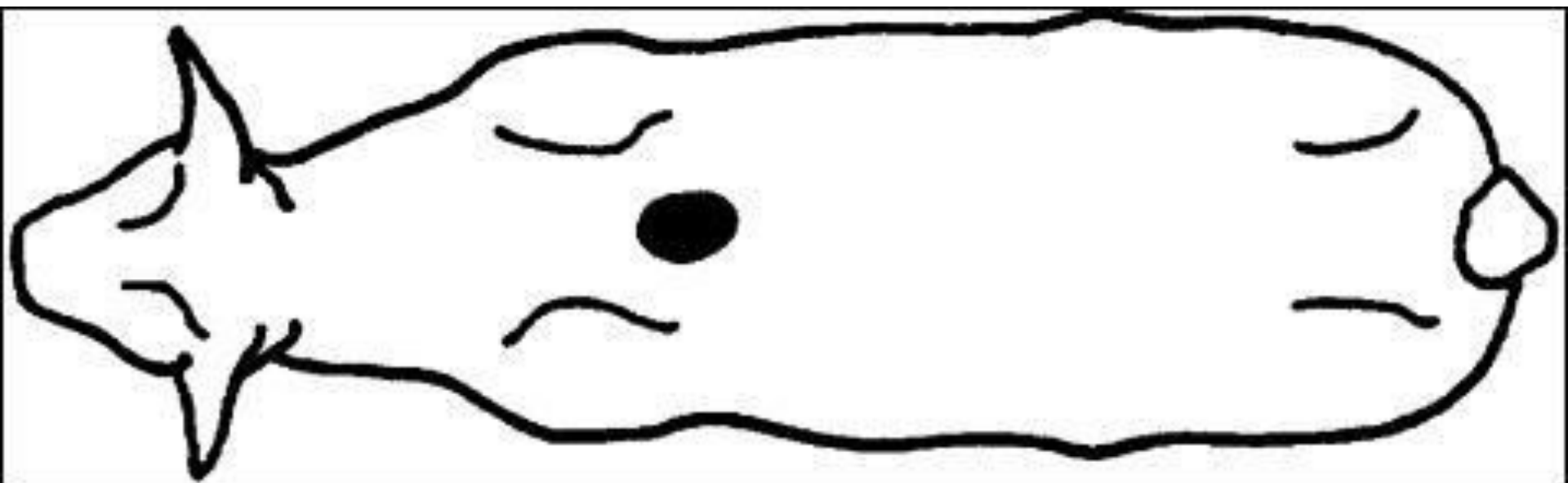
## Classification of Pesticides by Hazard

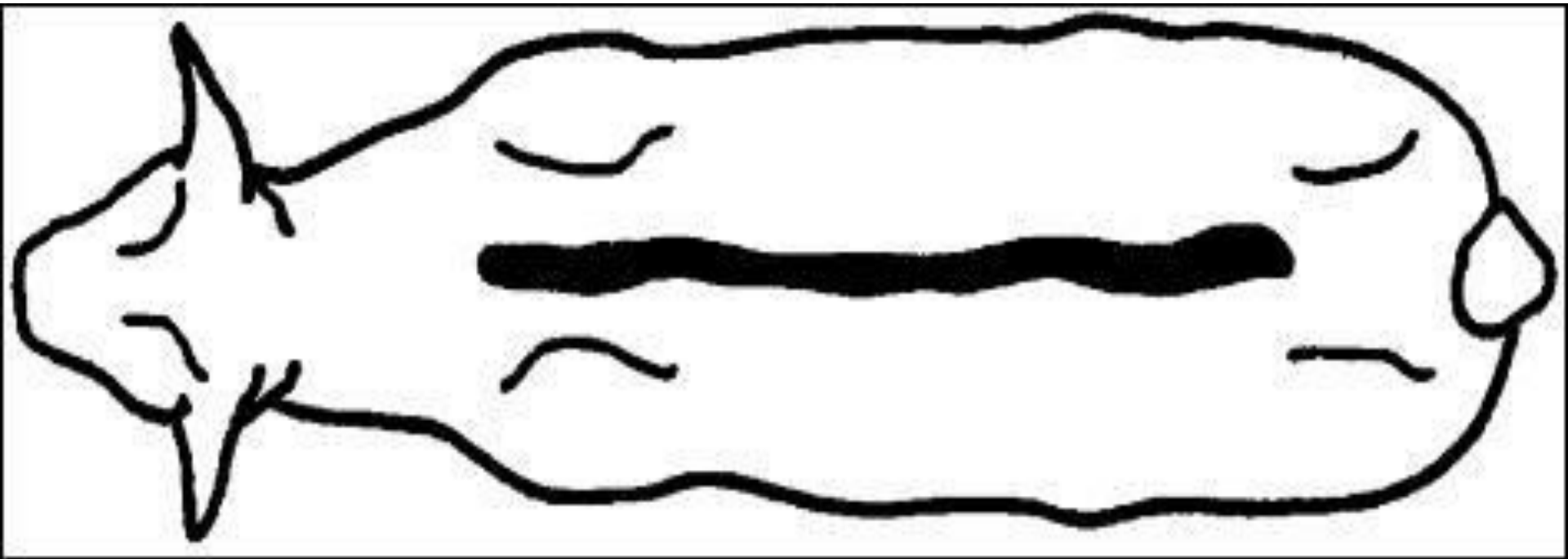
	LD <sub>50</sub> for the rat (mg/kg body weight)			
Class	Oral		Dermal	
	Solids	Liquids	Solids	Liquids
<b>Ia</b> Extremely hazardous	5 or less	20 or less	10 or less	40 or less
<b>Ib</b> Highly hazardous	5 - 50	20 - 200	10 - 100	40 - 400
<b>II</b> Moderately hazardous	50 - 500	200 - 2000	100 - 1000	400 - 4000
<b>III</b> Slightly hazardous	Over 500	Over 2000	Over 1000	Over 4000

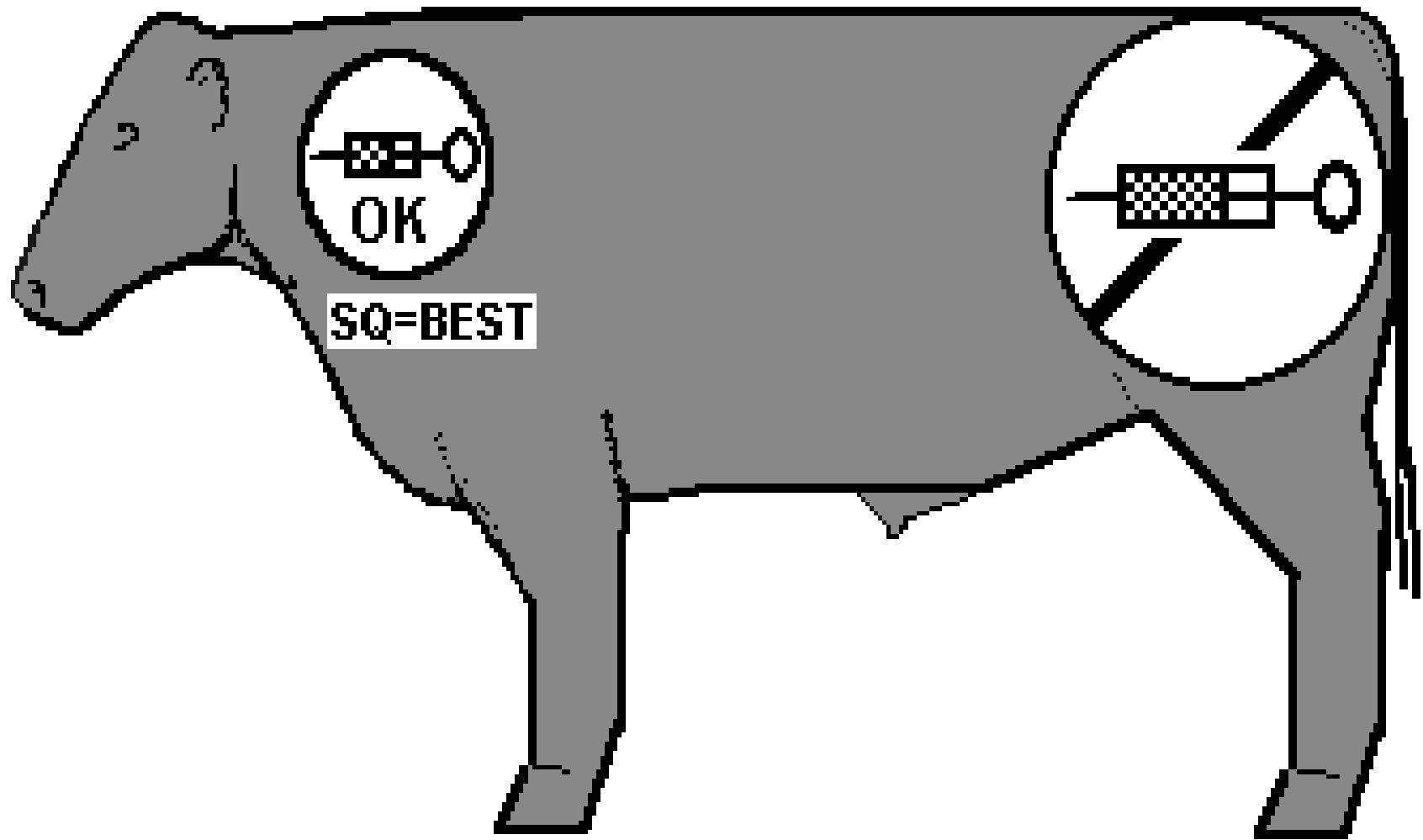
# Pharmaceutical classification











Never inject the rear. Don't Over Dose  
Avoid I.M. injections if possible  
Select sub-Q products when possible



# Modes of Action of Insecticides

```
graph TD; A[Modes of Action of Insecticides] --> B[Nervous System]; A --> C[Energy Production]; A --> D[Cuticle Production]; A --> E[Endocrine System]; A --> F[Water Balance];
```

Nervous System

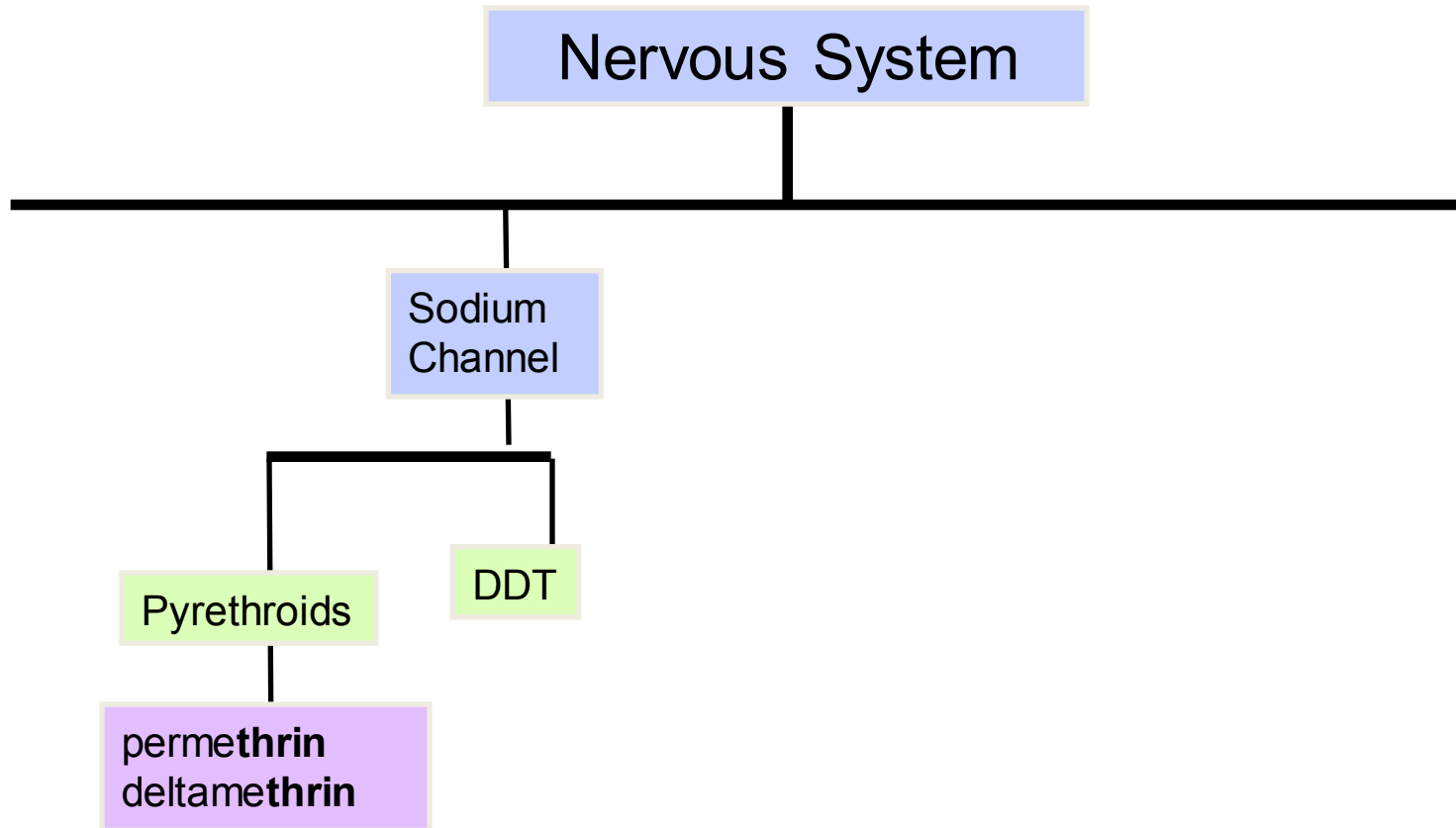
Energy Production

Cuticle Production

Endocrine System

Water Balance

# Insecticides that Affect the Nervous System



# Pyrethrins and Pyrethroids

- Pyrethrum -- dust derived from ground chrysanthemum flowers
- Pyrethrins -- chemicals within pyrethrum that have insecticidal properties

# Pyrethrins and Pyrethroids

Pyrethroids -- synthetically produced chemicals with similar chemistry and mode of action as pyrethrins, axonic poisons

- Type I
  - Short residual,
  - Fast flushing, and
  - Quick knockdown,
  - Negative temperature correlation: more effective at low temps
  - Ex.: Allethrin, d-phenothrin, resmethrin
- Type II
  - Long residual,
  - Slower flushing, and
  - Slower knockdown,
  - Better killing power than type 1
  - Positive temperature correlation
  - Ex.: Permethrin, cypermethrin, cyfluthrin, lambda-cyhalothrin
- Synergists -- used to deactivate mixed function oxidases (MFOs) within insects

# Pyrethroids Effects

- Action on Human System - Irritant
- Systemic Effects - Minimal
- Irritation Effects - Stinging, burning, itching, tingling, numbness of skin.

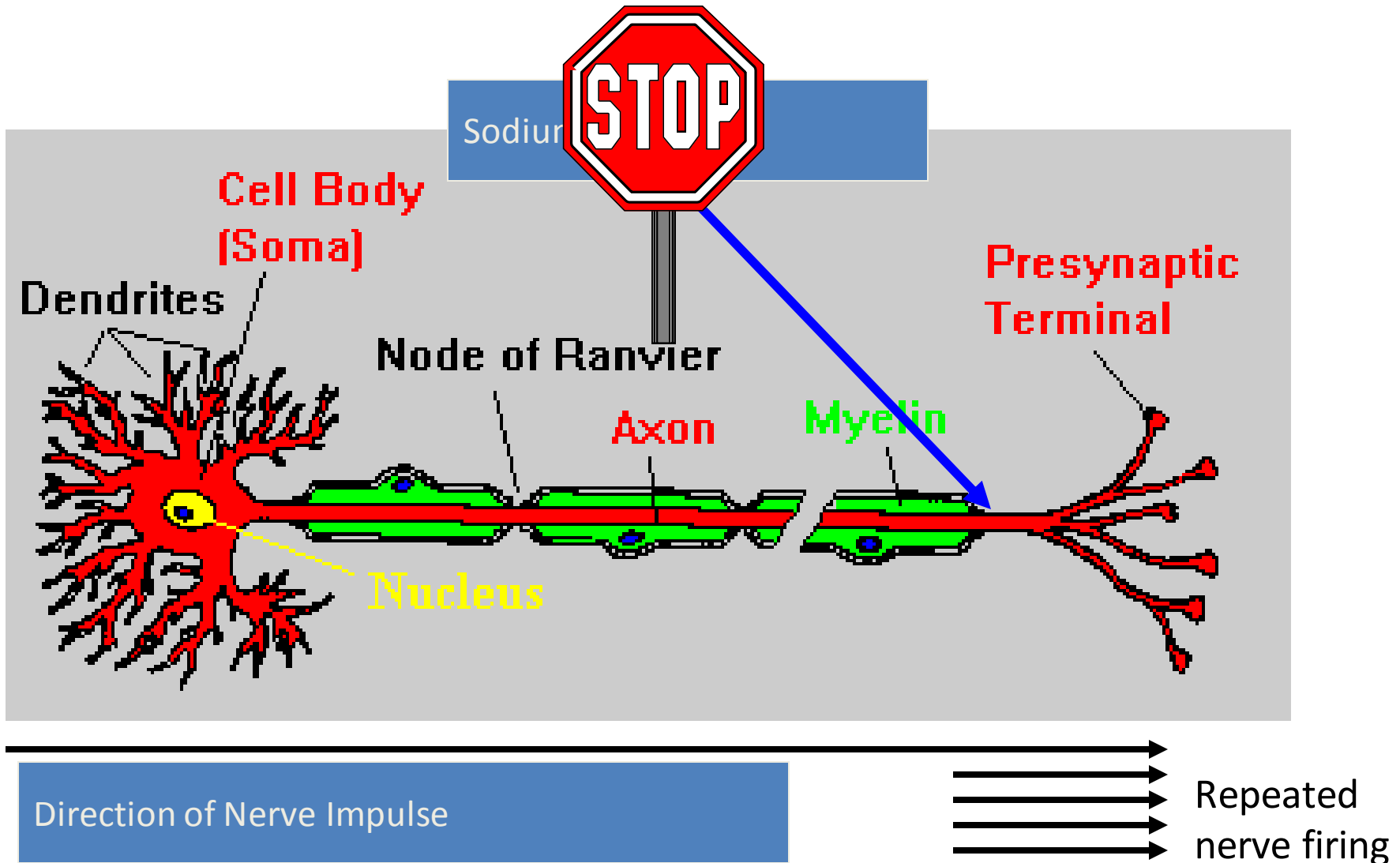
# MOA: Pyrethroids

- Axonic poisons
- Bind to a protein called the voltage-gated sodium channel
- Normally, the sodium channel opens, causing stimulation of the nerve and closes to end the nerve signal
- Pyrethroids bind to the sodium channel and prevent it from closing normally
- Result: continuous nerve stimulation
- Symptoms: Tremors, uncoordinated movement

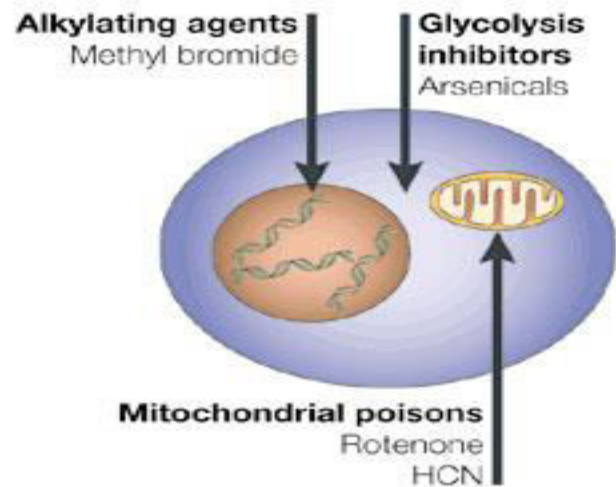
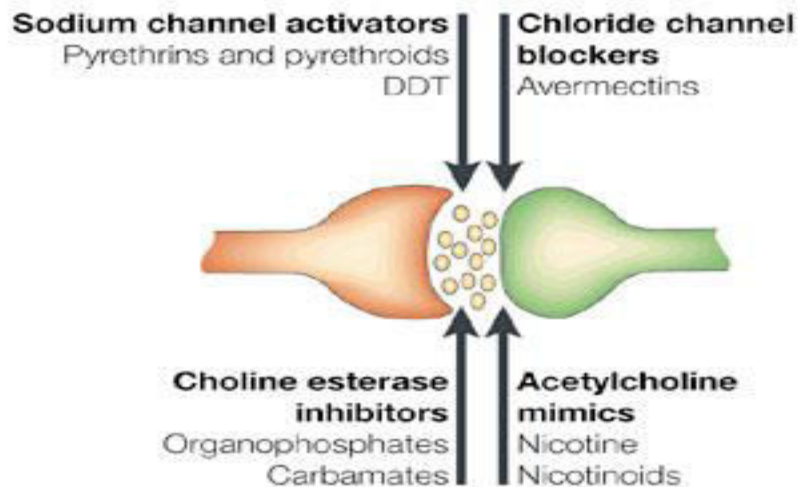
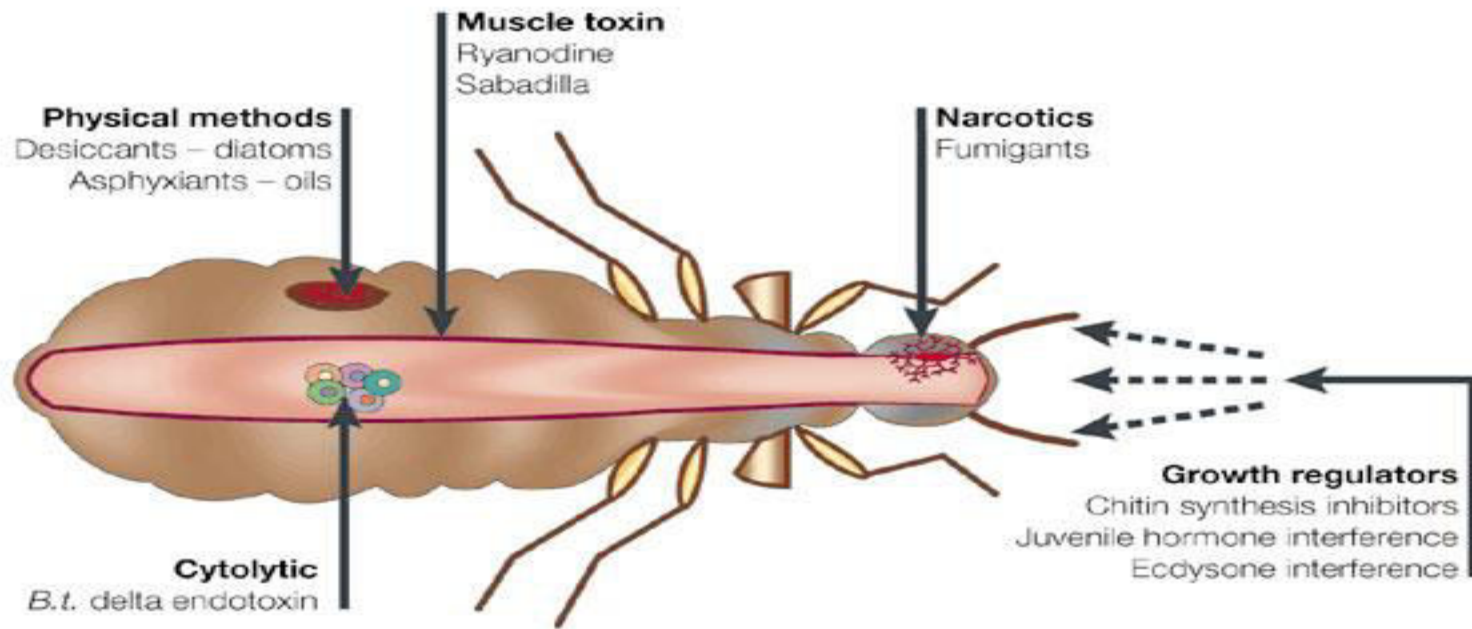
# Nervous System

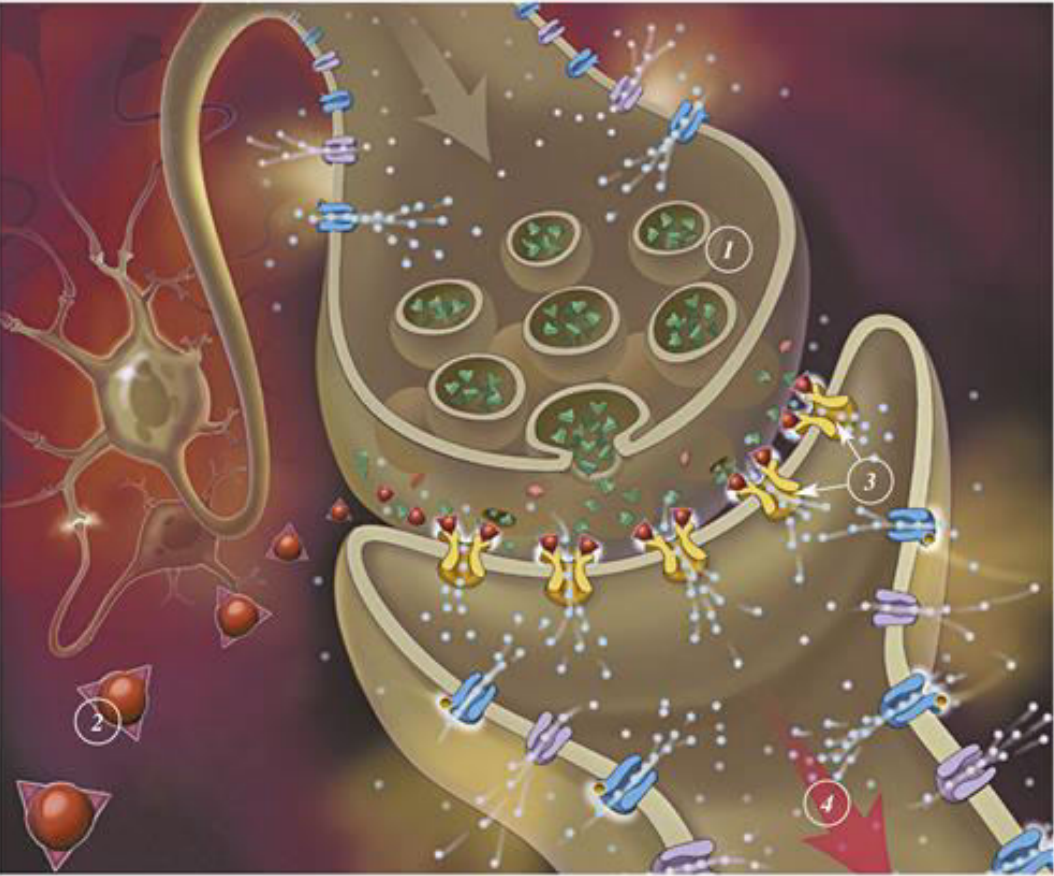
- Why does this happen?
- Let's look at a "normal" nerve impulse.

# Nerves and Pyrethroids



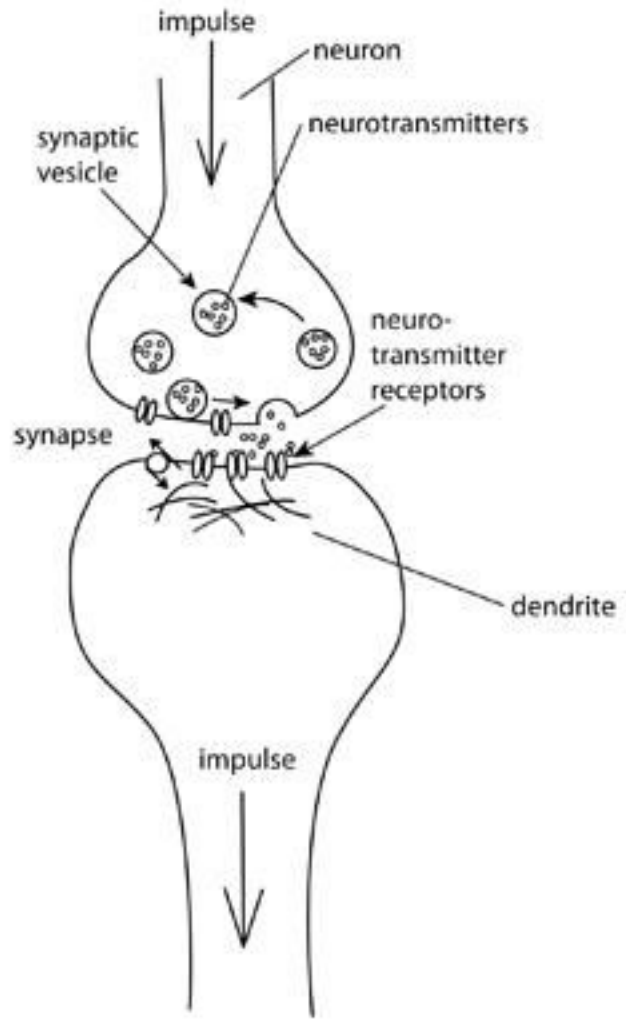




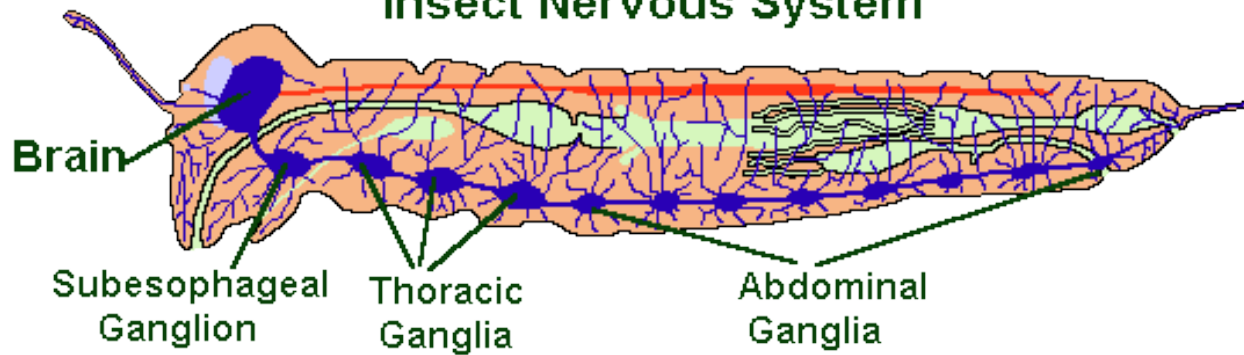


1 Vesicles of acetylcholine  
2 Imidacloprid

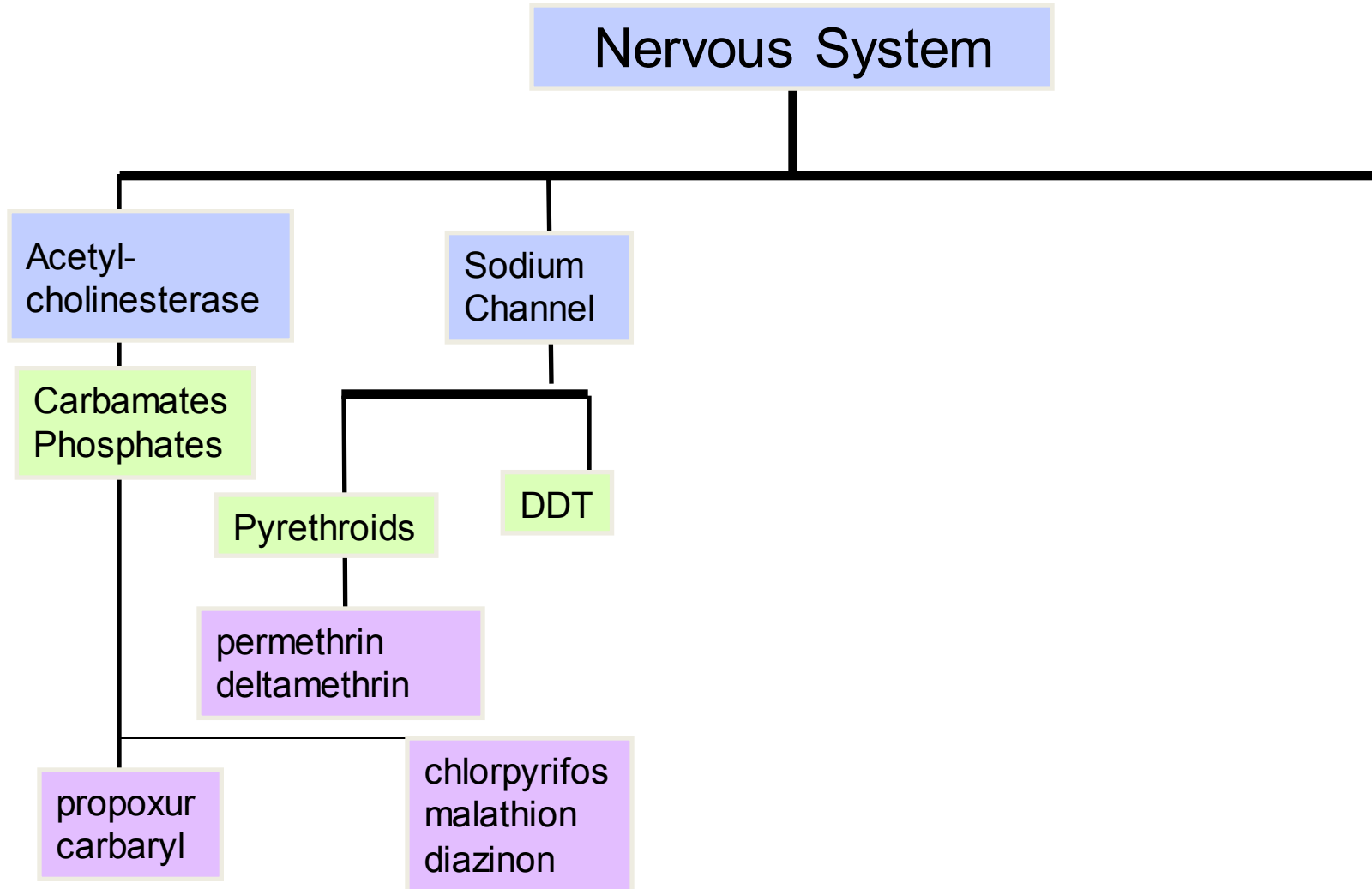
3 Nicotinic receptors blocked open  
4 Constant neuromuscular stimulation



## A Diagrammatic Representation of the Insect Nervous System



# Insecticides that Affect the Nervous System



# MOA: Carbamates and OPs

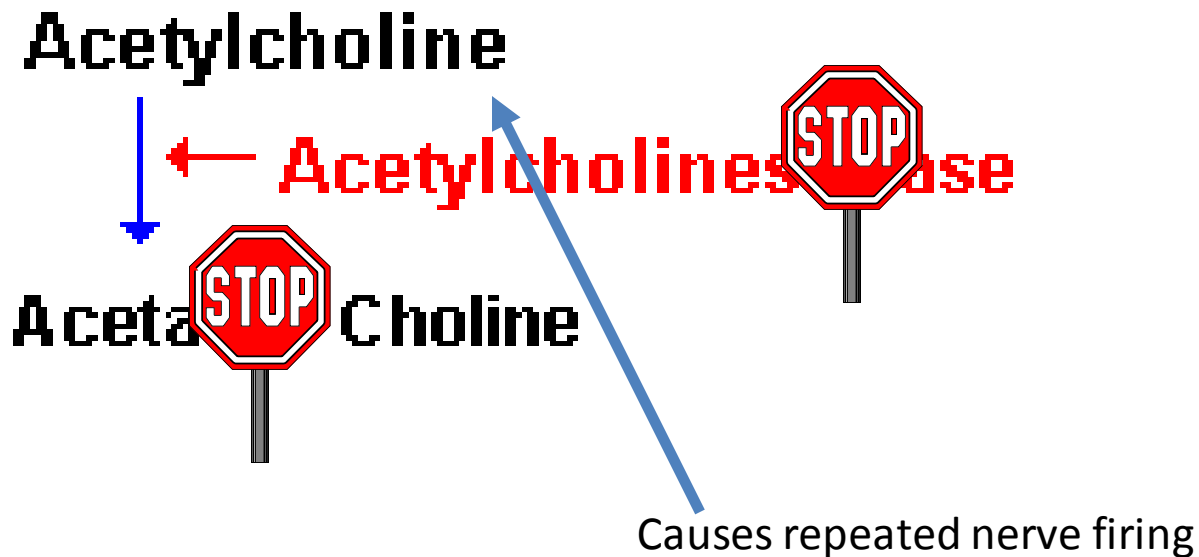
- Synaptic poisons
- Carbamates and organophosphorus insecticides bind to an enzyme called acetylcholinesterase (AChE)
- AChE is found at the nerve synapse
- AChE is designed to stop a nerve impulse after it has crossed the synapse

# MOA: Carbamates and OPs

- OPs and carbamates bind to AChE
- This prevents AChE from working (i.e., breaking down Ach)
- Therefore, nerve impulses continue to fire across the synapse
- Symptoms similar to pyrethroid poisoning—tremors and uncontrolled movement

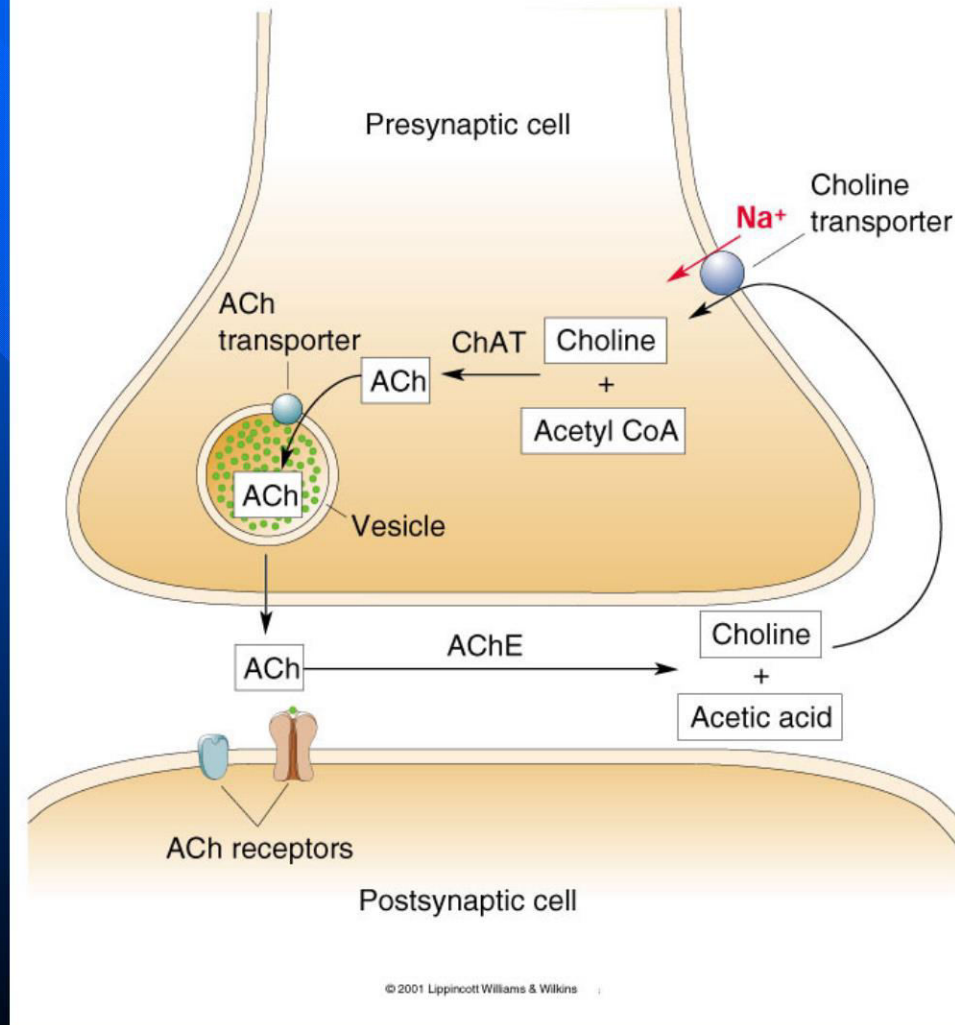
# Cholinesterase Inhibitors

- Organophosphates
- Carbamates



# Acetylcholine System

Figure 6.10  
The life cycle of ACh.





# Organophosphate Effects

- Action on Human System - Inhibits acetylcholinesterase enzyme in tissues.
- Systemic Effects - Headache, dizziness, weakness, shaking, nausea, stomach cramps, diarrhea, sweating.
- Irritation Effects - Minimal rashes, but readily absorbed through the skin.
- Delayed/Allergic Effects - Loss of appetite, weakness, weight loss, and general feeling

# N-Methyl Carbamates Effects

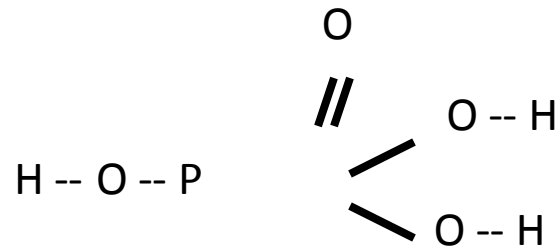
- Action on Human System - Reversible changes in acetylcholinesterase enzyme in tissues.
- Systemic Effects - Headache, dizziness, weakness, shaking, nausea, stomach cramps, diarrhea, sweating.
- Irritation Effects - Minimal rashes, but readily absorbed through the skin.
- Delayed/Allergic Effects - Loss of appetite, weakness, weight loss, and general feeling of sickness.
- Reversible inhibition of AChE

# Organophosphates and Carbamates

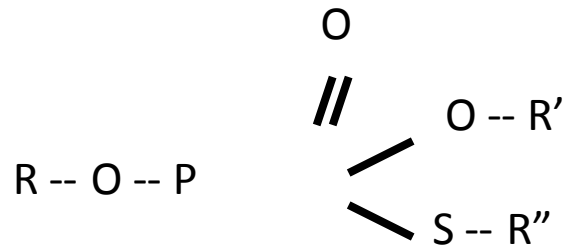
- Organophosphates
    - Chlorpyrifos\*
    - Diazinon\*
    - Trichlorfon\*
    - Parathion\*
  - Carbamates
    - Carbaryl (Sevin)
    - Propoxur (Baygon)\*
- Chemicals which are derived from phosphoric and carbamic acid and bond with cholinesterase
- Acute toxicity
  - Not persistent
  - Hyper-excitation
  - Insect flips on back with legs twitching
  - Sulfur in formulation
  - often causes strong odor

\*EPA hit list or not common in UPM

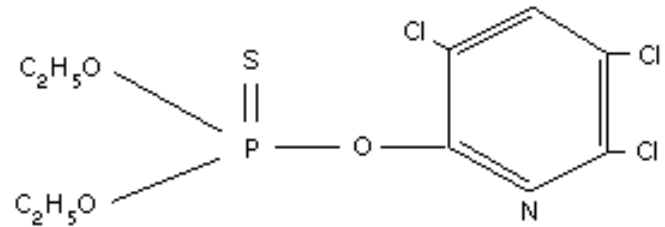
# Organophosphates



Phosphoric Acid

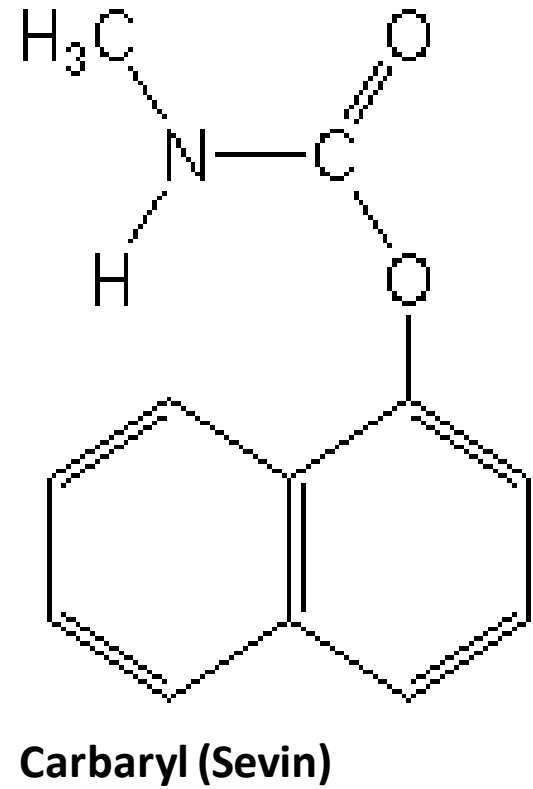
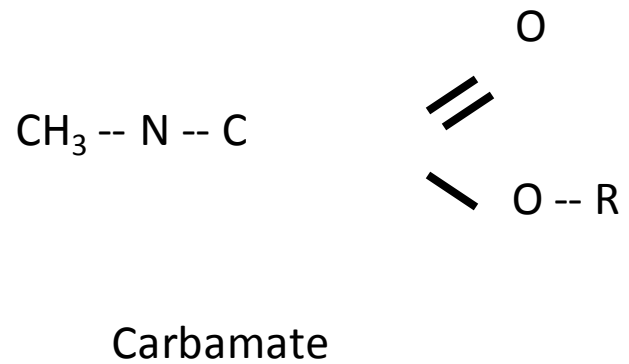
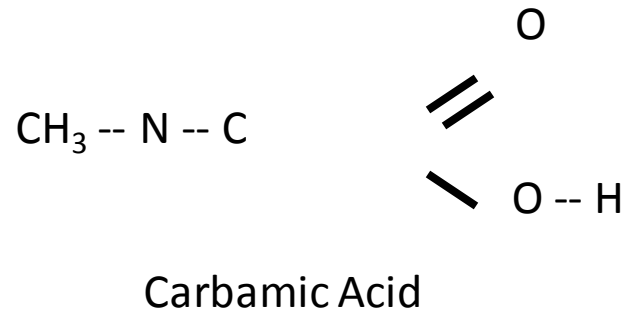


Phosphorothioate

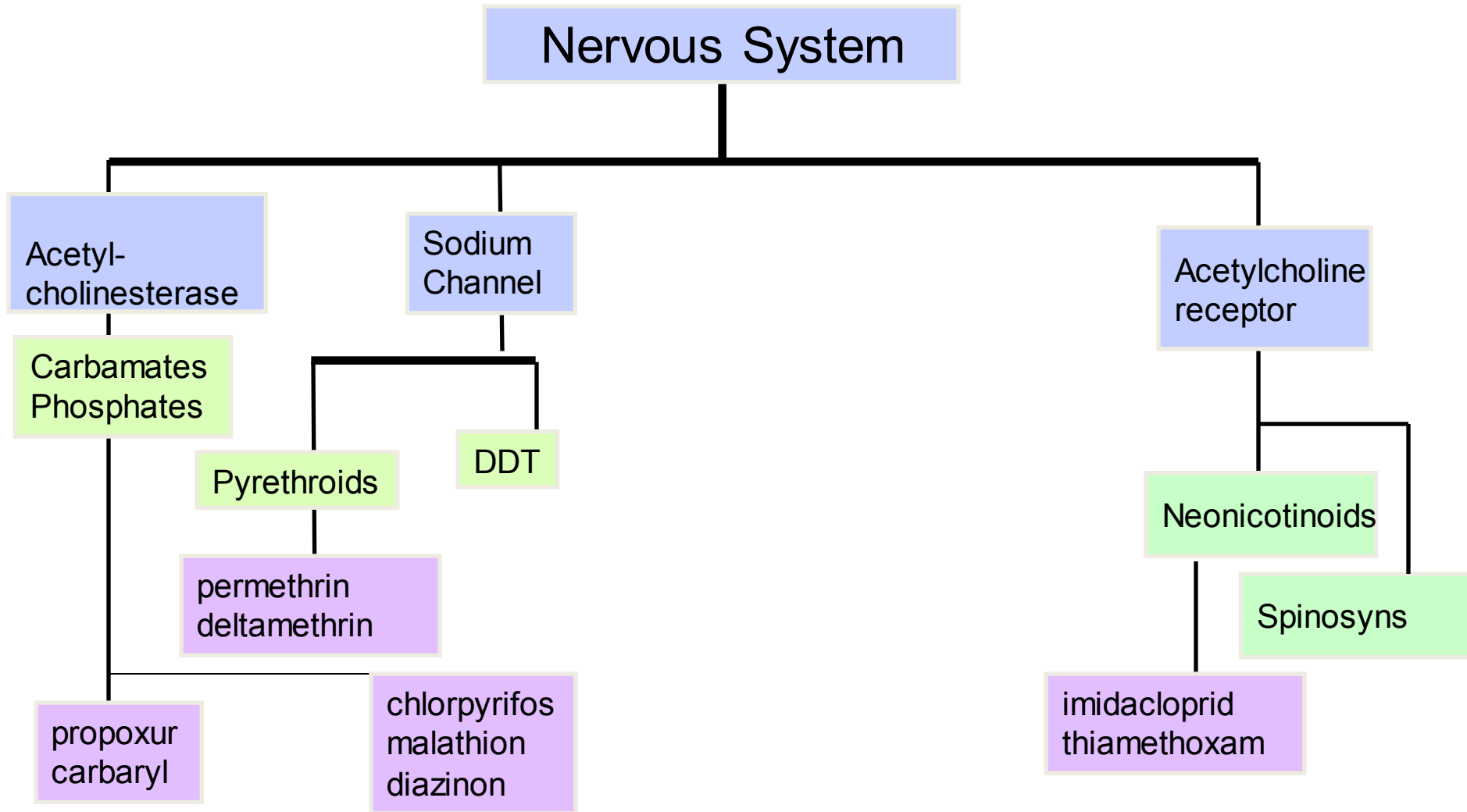


Chlorpyrifos ((Dursban))

# Carbamates

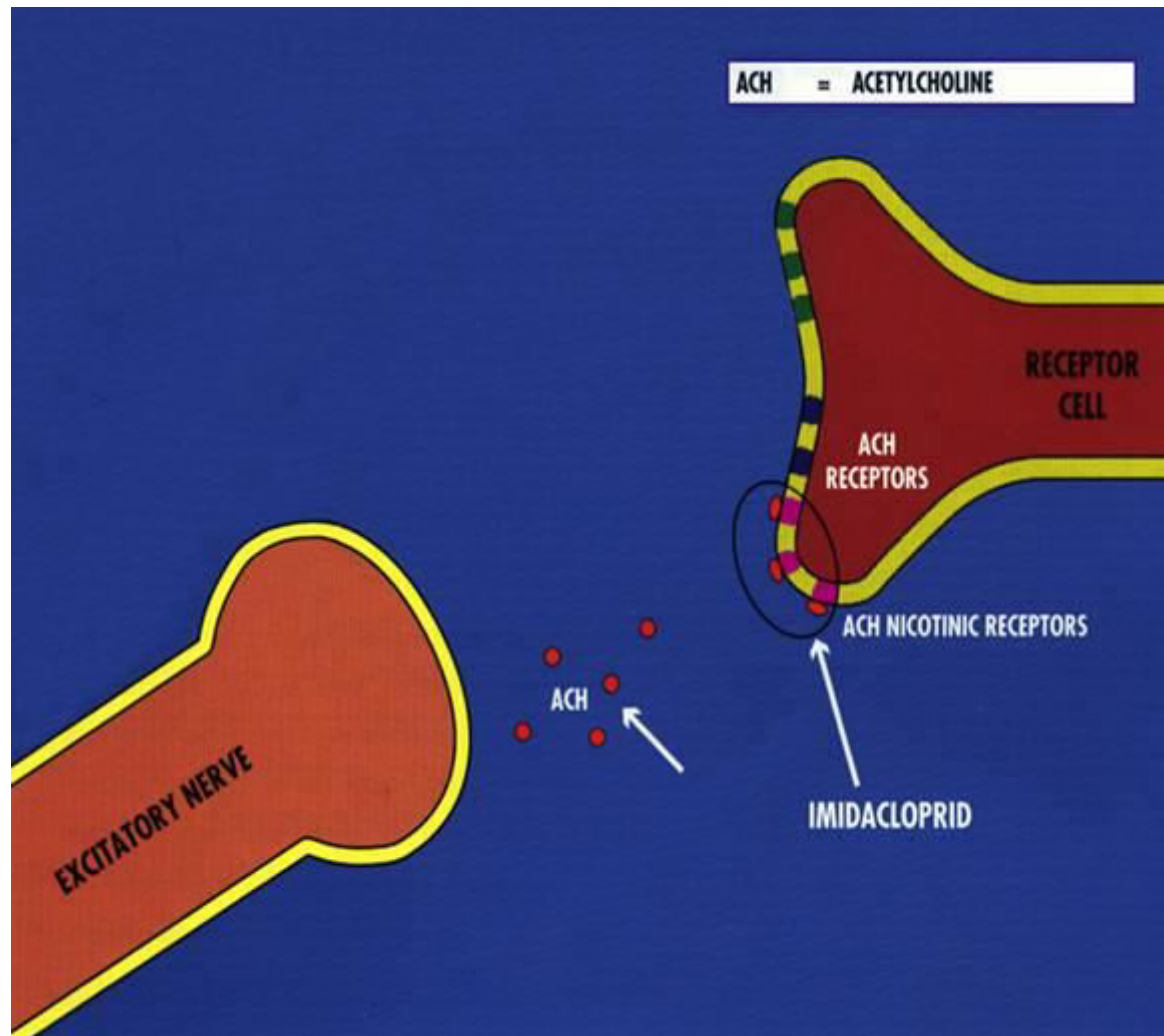


# Insecticides that Affect the Nervous System



# Acetylcholine Receptor

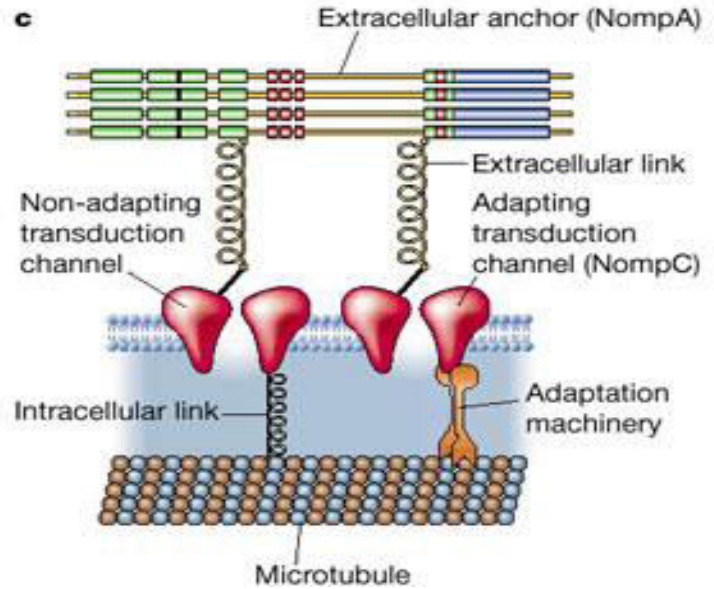
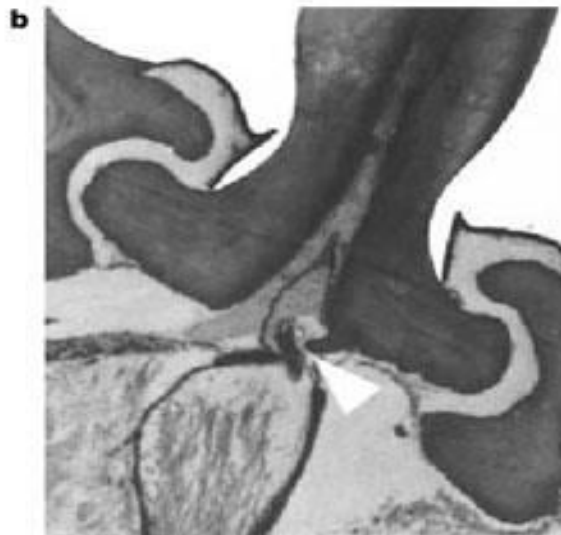
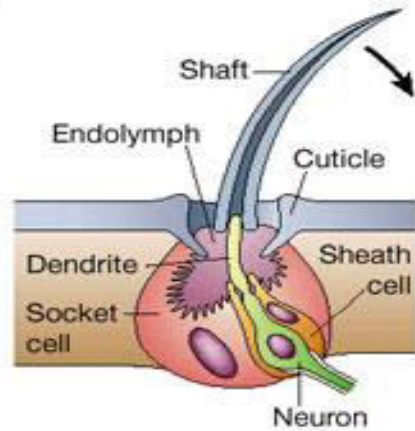
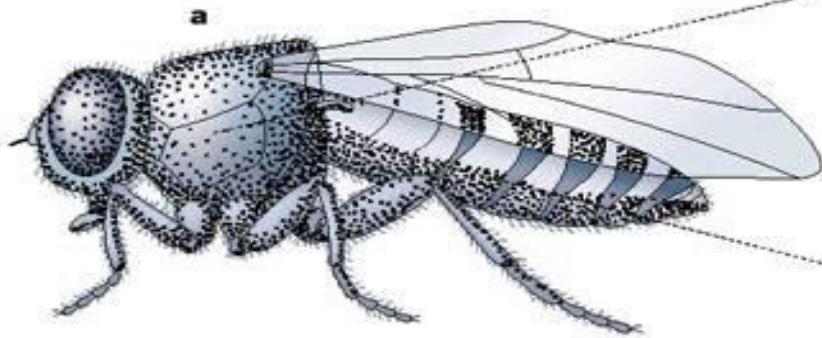
- Mimics acetylcholine on the receptor
  - Nicotinic receptor is a type of ACh receptor that is sensitive to nicotine
- Cannot be broken down by AChE
- Imidacloprid turns nerve impulse on but AChE does not degrade it
- Similar overstimulation as seen with OPs and Carbs



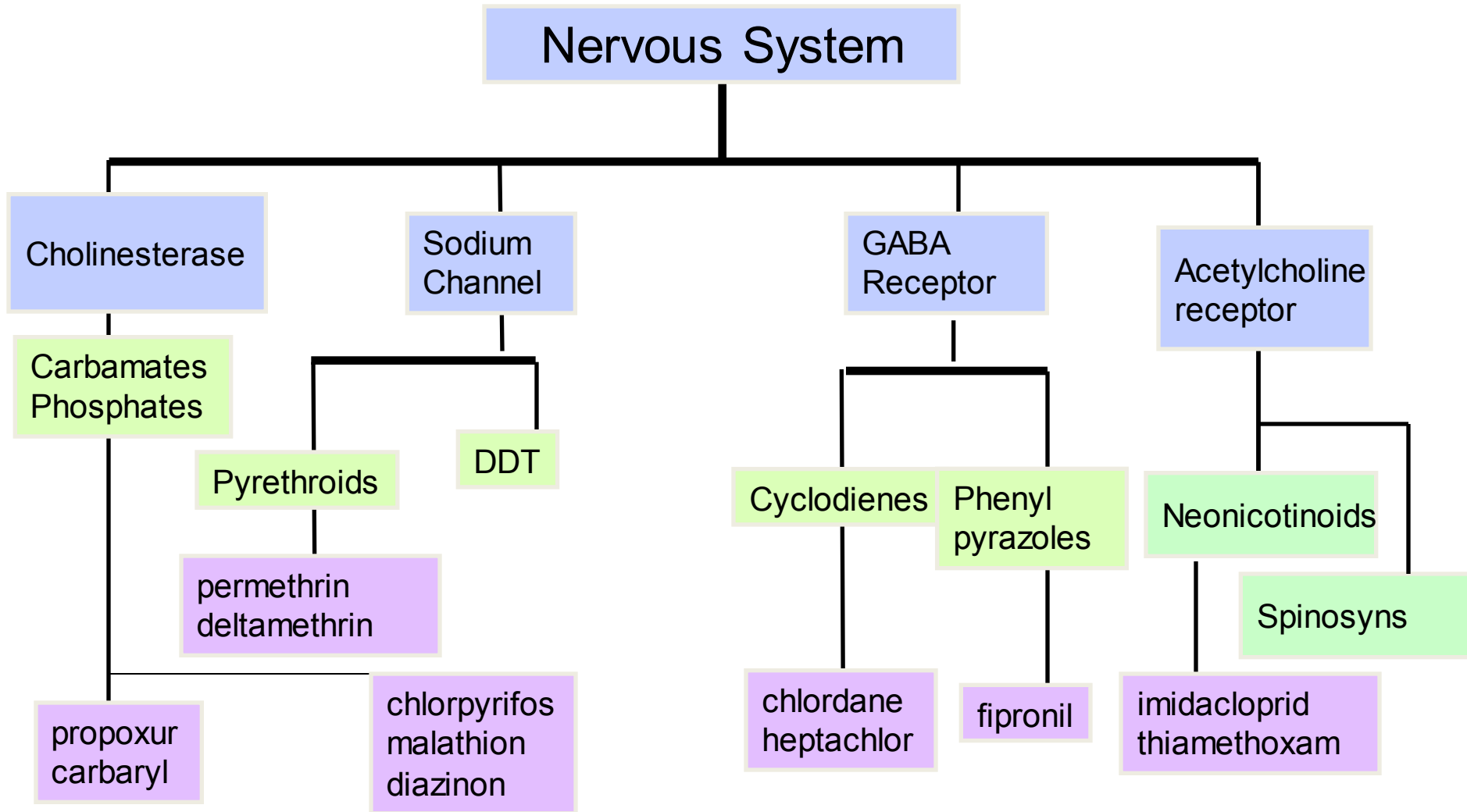
# Neonicotinoids

- Imidacloprid (subgroup: pyridylmethanamine)
  - Advantage – pet treatment
  - Merit -- turf ornamentals
    - Water soluble
    - Systemic in plants
  - Premise – termites
    - Affects insects first by paralyzing mouthparts
  - Bayer Advantage OTC
- Thiamethoxam (subgroup: nitroguanidine)
  - Used in crops
  - Working on urban and landscape/turf/ornamentals label
- (Subgroup: nitromethylene)





# Insecticides that Affect the Nervous System

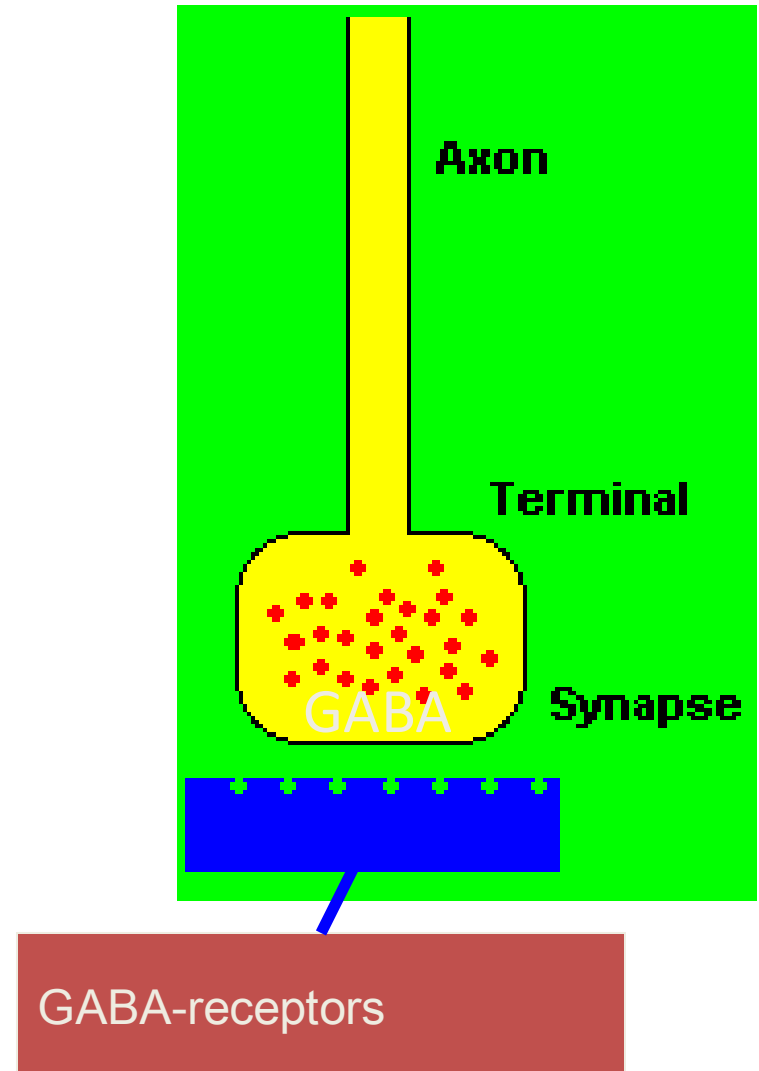
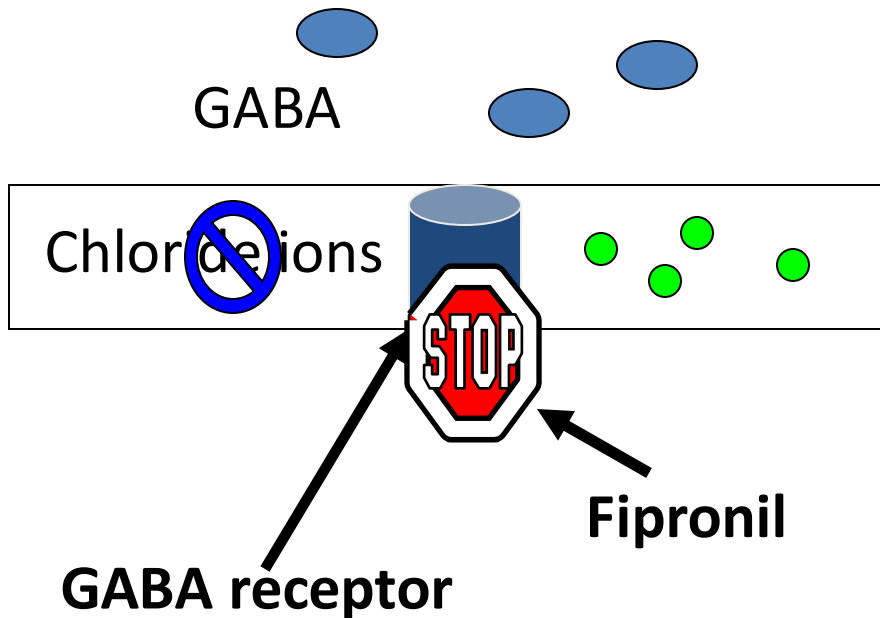


# MOA: GABA Antagonist

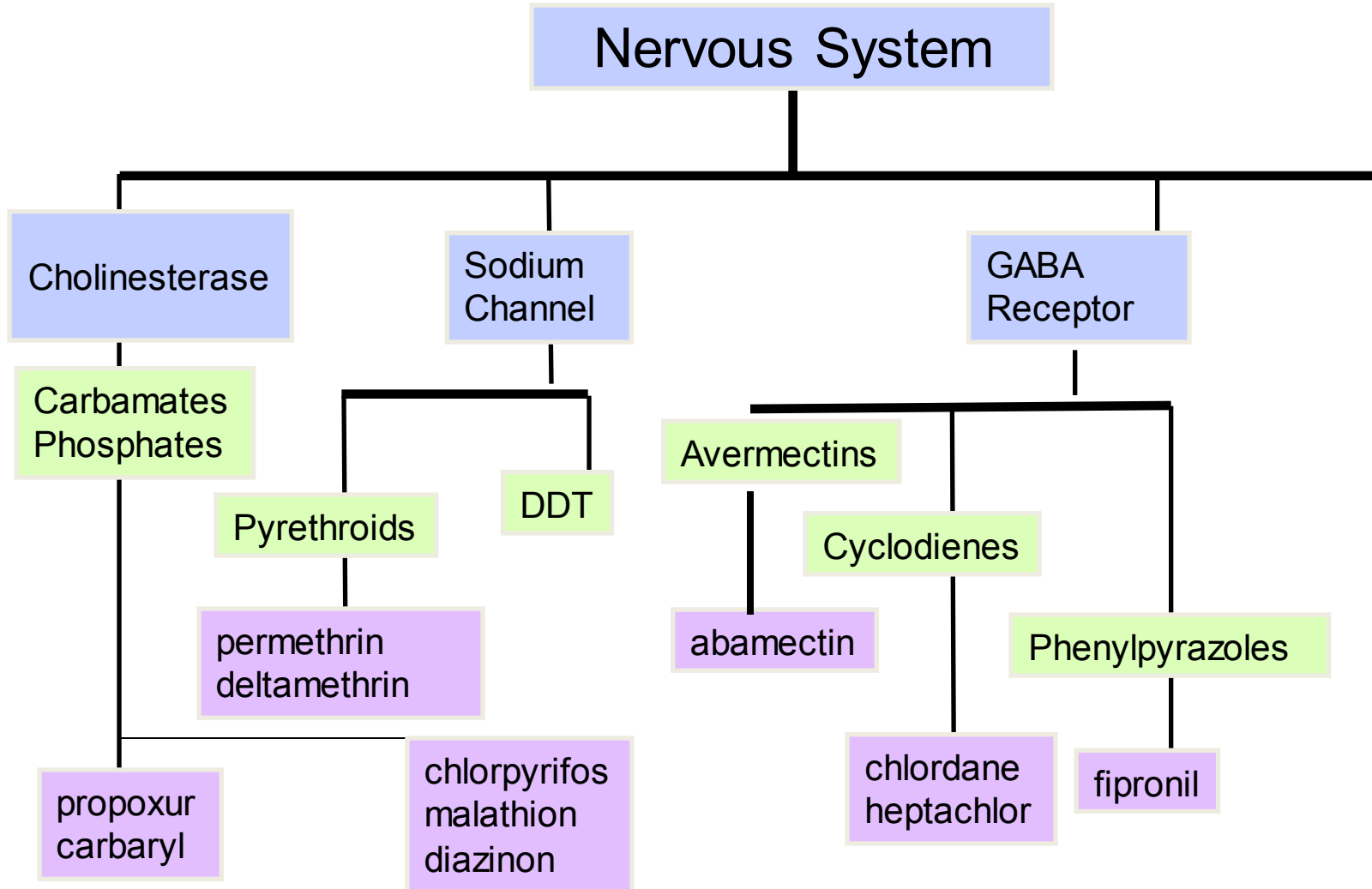
- Phenylpyrazole (fipronil), cyclodienes
- Antagonists of GABA activated chloride channels
- GABA Antagonists: chemicals that bind to but do not activate GAMMA-AMINOBUTYRIC ACID receptors, thereby blocking the actions of endogenous GAMMA-AMINOBUTYRIC ACID or GAMMA-AMINOBUTYRIC ACID agonists.
- GABA can't bind to receptor
- Doesn't activate channel (doesn't open)
- Interferes with (prevents) the passage of chlorine ions through the channel.
- Concerns with cross resistance with other GABAergic insecticides

# GABA Receptor in Central Nervous System

- Phenylpyrazoles or
- Fiproles



# Insecticides that Affect the Nervous System

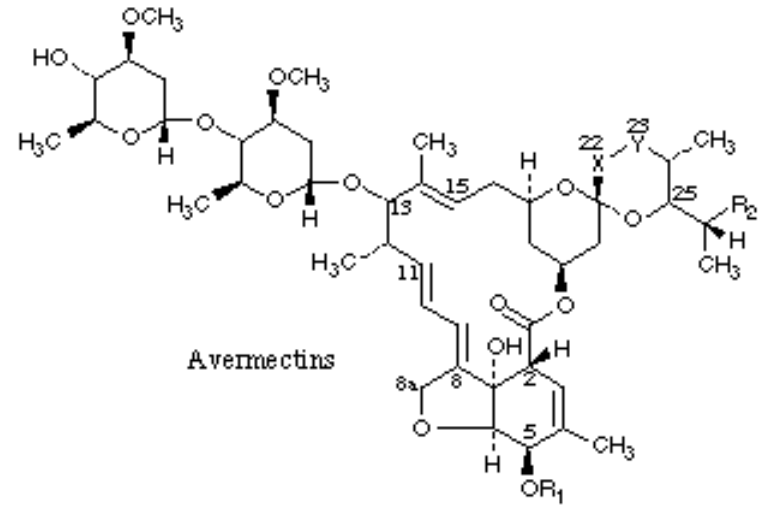


# MOA: GABA Agonist

- Avermectins
- Bind to GABA (Gamma-Amino-Butyric Acid gated chloride channel
- Opens channel
- Chloride influx
- Cannot reach threshold for action potential
- Causes membrane to hyperpolarize, making it less excitatory, decreasing nerve transmission
- Result: flaccid paralysis and death

# Avermectins

- Abamectin
  - Avert -- cockroaches
  - Advance -- ants



Produced from soil microbials. Stomach poison for ants and cockroaches

slow acting

low toxicity to mammals

# Modes of Entrance into Insect

- Contact - dermal – through the skin
- Stomach - oral – through the mouth
- Respiration - inhalation through the nose or gills
- Systemic - combination of above



# Mode of Toxicity in Insects

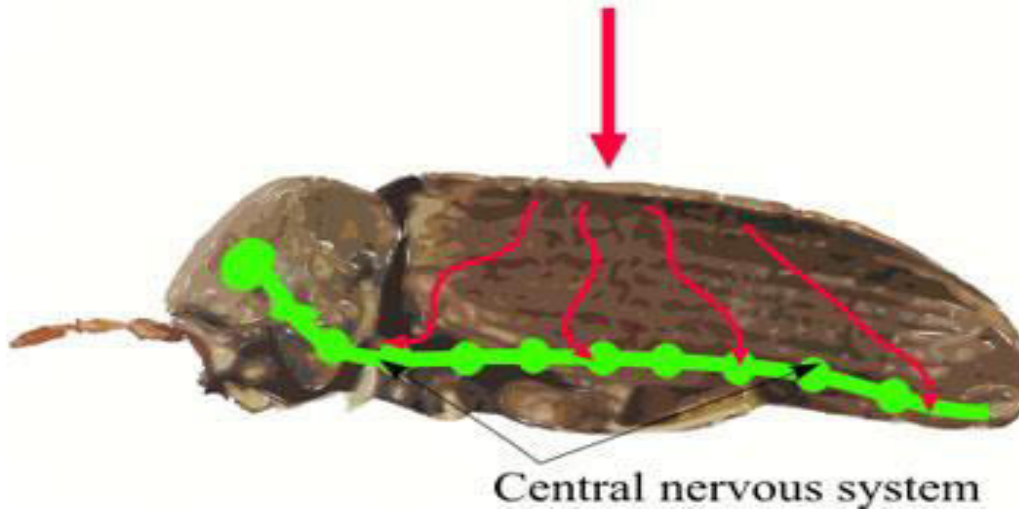
- Physical poison
- General protoplasmic poison
- Cellular enzyme poison
- Nerve poison
- Growth regulator
- Disease causing agent
- Repellant

# Toxicity to humans or nontarget organisms

- Most insecticides have the capacity to affect nontarget organisms
- Same as previously discussed
  - Highly toxic –  $LD_{50}$  0 – 50 mg/kg
  - Moderately toxic -  $LD_{50}$  50 – 500 mg/kg
  - Low toxicity -  $LD_{50}$  500 – 5,000 mg/kg
  - Nontoxic -  $LD_{50}$  <5,000 mg/kg

# CONTACT INSECTICIDES

Contact insecticide





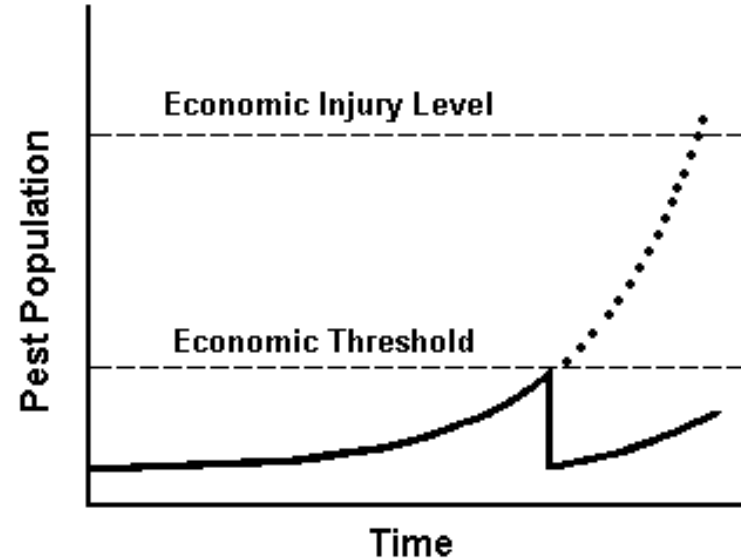
# Avert Kill

- 22 hours to nerve effects
- 40 hours to kill

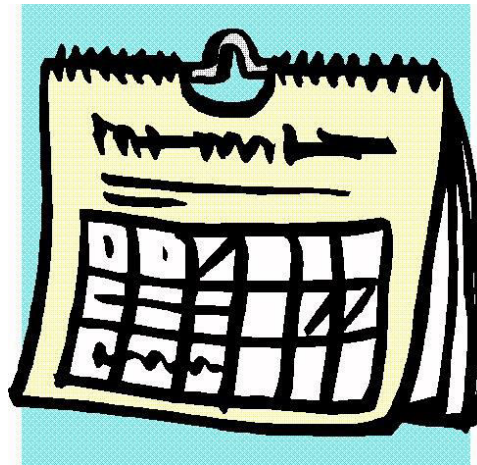


# When to apply?

- Thresholds



- Calendar applications



# Reasons for lack of Commercial Development

- Perceived as old fashioned
- Lack of representation on official lists
- Not as dramatic effects as synthetic insecticides
- Inactivation by exposure to air and light
- Problems due to seasonal availability
- Lack of quantitative information regarding dosages
- Lack of quantitative information regarding toxicity



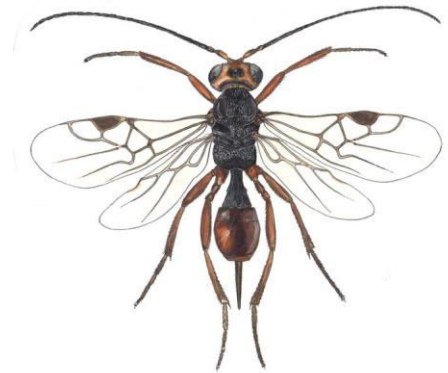


Affect synaptic transmission



# The Pesticide Treadmill

- Pest resurgence
- Secondary pest outbreaks
- Pesticide resistance



وَعَلَّمَ آدَمَ الْأَسْمَاءَ كُلَّهَا ثُمَّ عَرَضَهُمْ

عَلَى الْمَلَائِكَةِ فَقَالَ أَنْبِئُونِي بِأَسْمَاءِ

هَٰؤُلَاءِ إِنْ كُنْتُمْ صَادِقِينَ ﴿٣٦﴾ قَالُوا

سُبْحٰنَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ

أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴿٣٧﴾

# Toxicity to insects natural enemies

- Most insecticides have the potential to affect populations of beneficial insects.

# Environmental hazard

- Environmental hazard of insecticides is generally evaluated as a function of persistence often compared to effectiveness

# Resistance/Resurgence Hazard

- The hazard of populations developing resistance and resurging is evaluated for most insecticides





# شكراً لحسن الإستماع

Thank  
You!



*To all professors of parasitology  
who taught me.*



# Pesticides

## Fumigants

Phosphine

Ethylene dibromide/  
dibromochloropropane

## Fungicides

Hexachlorobenze

Pentachlorophenol

**Phthalamides**

-Captan, Folpet

**Dithiocarbamates**

-Maneb\*, Ziram

## Herbicides

**Bipyridyls**

-Paraquat\*, Diquat

**Phosphomethyl amino acids**

-Glyphosate

**Chloroacetanilides**

-Alachlor

**Chlorophenoxy Compounds**

-2,4-dichlorophenoxyacetate

## Rodenticides

Zinc Phosphide

Fluoroacetate Derivatives

$\alpha$ -naphthyl thiourea

**Anticoagulants**

-Diphacinone,

Bromdialone

## Insecticides

### **Anticholinesterases**

-Organophosphates  
-Parathion,  
Chlorpyrifos\*  
-Carbamates  
-Aldicarb, Methomyl\*

### **Avermectins**

-Ivermectin

### **Botanicals**

-Nicotine  
-Rotenoids  
-Rotenone\*,  
Deguelin

### **Organochlorines**

-Cyclodienes  
-Dieldrin\*, Heptachlor  
-Dichlorodiphenylethanes  
-DDT\*, methoxychlor  
-Cyclohexanes  
-Lindane,  $\beta$ -HCH

### **Pyrethroids**

-Type I  
-Permethrin\*  
-Type II  
-Cypermethrin,  
Deltamethrin\*

### **Other**

-Nitromethylene  
-Chloronicotinyl  
-Phenylpyrazole