

Strategies for control of parasite vectors and impact on ecosystems

International Master
TU N°02, Infectiology
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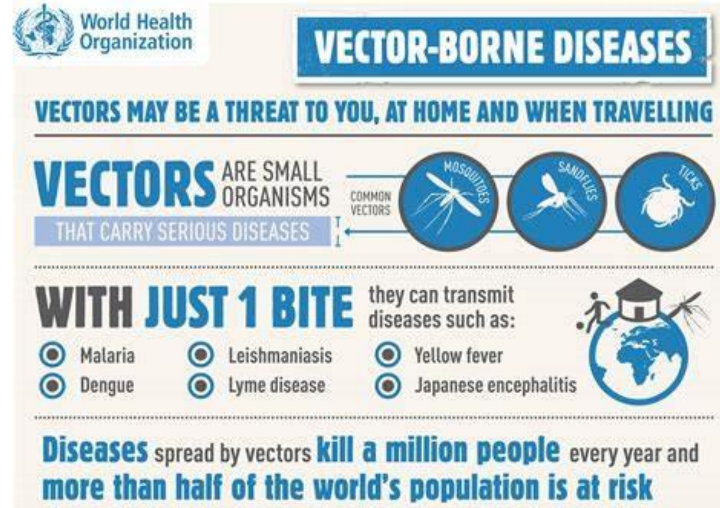
Vector-borne diseases



→ human diseases caused by parasites, viruses and bacteria that are transmitted by vectors

→ More than 17% of all infectious diseases

→ Causing more than 700 000 deaths annually

→ Many vector-borne diseases can be prevented, through protective measures, and community mobilization

→ The burden of these diseases → highest in tropical and subtropical areas affecting the poorest populations

→ Distribution of vector-borne diseases

→ Determined by a complex set of demographic, environmental and social factors including travels, trade, urbanization, …

What are parasite vectors?

→ Parasite vectors are hematophagous Arthropods that

→ ensure the active biological or mechanical transmission of parasites between humans, or from other vertebrates to humans *(Rodhain et Pérez, 1985)*

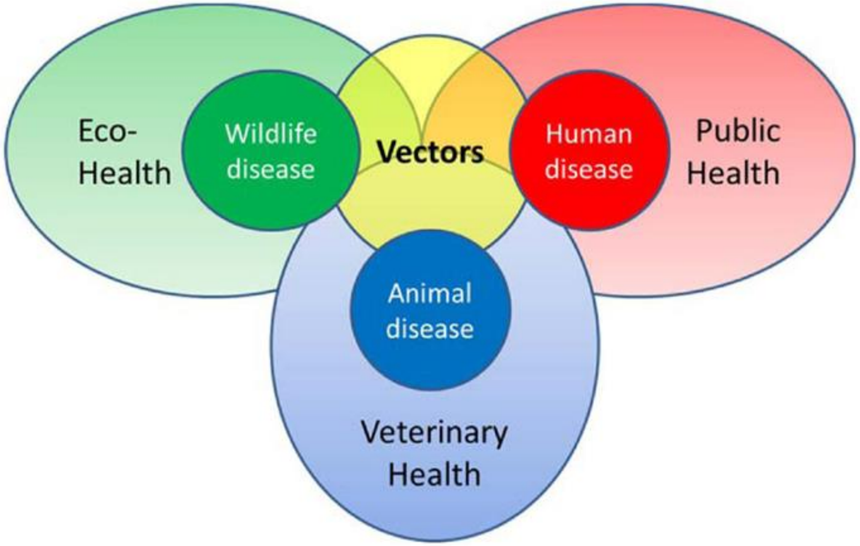
→ Ingest parasites during a blood meal from an infected host (human or animal) and later transmit it into a new host, after the parasite has replicated

→ Intermediate hosts such as snails in the life cycle of schistosomiases are not vectors because they only have a passive role (parasites go in and go out them without an active action from their part)

→ Often, once a vector becomes infectious

→ Able to transmit the parasite for the rest of its life during each subsequent bite/blood meal

Parasitic diseases transmitted by vectors



- Malaria → transmitted by Anophelinae mosquitoes
  → 219 million cases globally
  → Results in more than 400,000 deaths every year
  (most deaths occur in children under the age of 5 years)

- Chagas disease → transmitted by triatomine bugs

- Leishmaniasis → transmitted by sandflies (*Phlebotomus sp/Lutzomia sp*)

- Human African trypanosomiasis → transmitted by Tse-tse flies (*Glossina sp*)

- Lymphatic filariasis → transmitted by *Aedes* mosquitoes

- Onchocerciasis → transmitted by black flies (*Simulium sp*)

Viral diseases transmitted by vectors

- Dengue → the most prevalent viral infection
→ transmitted by *Aedes* mosquitoes
→ more than 3.9 billion people in over 129 countries are at risk, with an estimated 96 million symptomatic cases and an estimated 40,000 deaths every year

Aedes aegypti

Aedes albopictus

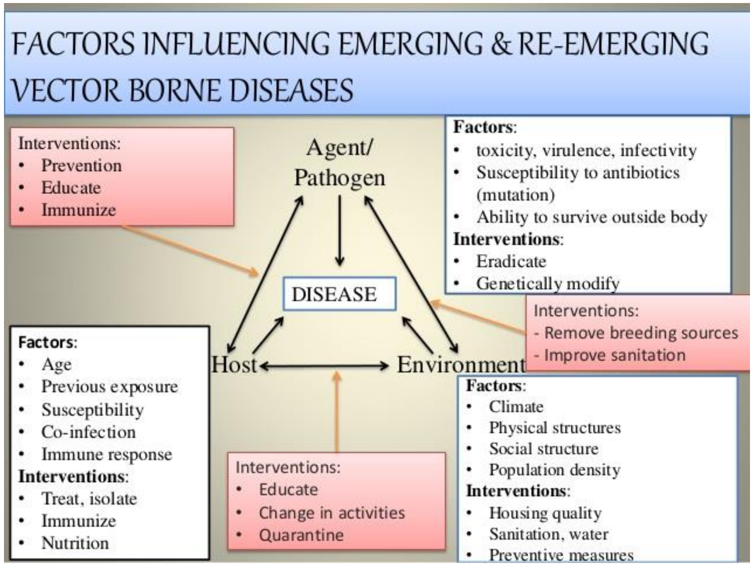
- Chikungunya fever
- Zika virus fever
- Yellow fever
- West Nile fever
- Japanese encephalitis (all transmitted by mosquitoes)
- Tick-borne encephalitis (transmitted by ticks)

Non-exhaustive list of vector-borne diseases according to their vector

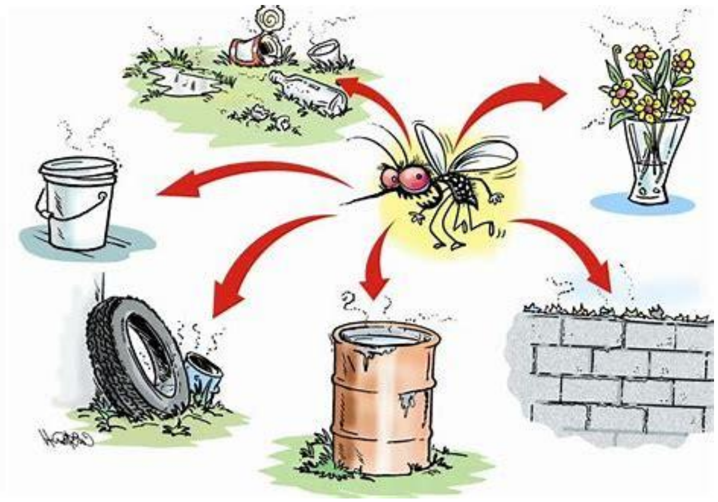
Vector		Disease caused	Type of pathogen
Mosquito	*Aedes*	Chikungunya	Virus
		Dengue	Virus
		Lymphatic filariasis	Parasite
		Rift Valley fever	Virus
		Yellow Fever	Virus
		Zika	Virus
	Anopheles	Lymphatic filariasis	Parasite
		Malaria	Parasite
	Culex	Japanese encephalitis	Virus
		Lymphatic filariasis	Parasite
		West Nile fever	Virus
Blackflies		Onchoceriasis (river blindness)	Parasite
Fleas		Plague (transmitted from rats to humans)	Bacteria
		Tungiasis	Ecto parasite
Lice		Typhus	Bacteria
		Louse-borne relapsing fever	Bacteria
Sandflies		Leishmaniasis	Parasite
		Sandfly fever (phlebotomus fever)	Virus
Ticks		Crimean-Congo haemorrhagic fever	Virus
		Lyme disease	Bacteria
		Relapsing fever (borreliosis)	Bacteria
		Rickettsial diseases (eg: spotted fever and Q fever)	Bacteria
		Tick-borne encephalitis	Virus
		Tularaemia	Bacteria
Triatome bugs		Chagas disease (American trypanosomiasis)	Parasite
Tsetse flies		Sleeping sickness (African trypanosomiasis)	Parasite

Present situation in the world

→ Since 2014, major outbreaks of:
→ dengue
→ malaria
→ chikungunya
→ yellow fever
→ Zika
→ afflicted populations (high mortality) and saturated health systems in many countries



→ Other diseases such as leishmaniasis and lymphatic filariasis
→ cause chronic suffering
→ life-long morbidity
→ disability
→ occasional stigmatization



Controlling the vectors

Sanitization methods

Objectives :

→ Limiting the proliferation of arthropods populations

→ Reducing contacts between arthropod populations and human population

→ Need hygienic measures

Means :

→ Risk identification

→ Monitoring and surveillance of vectors

→ Trapping systems for capturing vectors

→ Track the presence of a vector among a population

→ Detect the introduction of an exotic vector in an area previously free of this vector

→Track the population diffusion after insecticide use

→ Determine vector abundance in order to appreciate the risk of parasite transmission

→ Study of transmission models

→ Theoretical density threshold below which parasite transmission is not possible anymore

Controlling the vectors

Sanitization methods

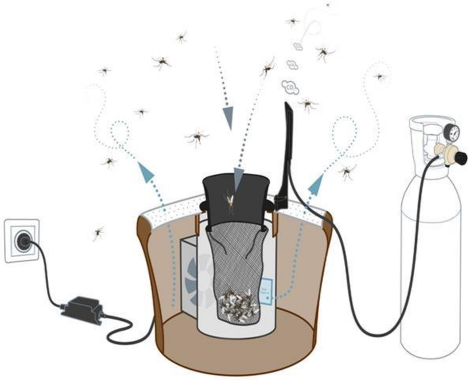
→ Risk identification

→ Monitoring and surveillance of vectors

→ Trapping systems for capturing vectors

→ Light traps (mosquitoes and sandflies)

→ CO_2 traps (mosquitoes)



Controlling the vectors

Sanitization methods

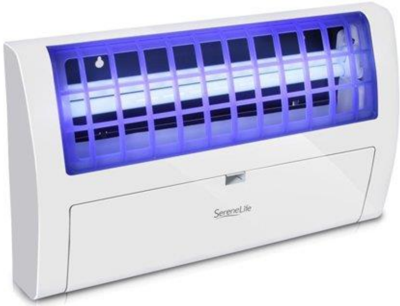
→ Risk identification

→ Monitoring and surveillance of vectors

→ Trapping systems for capturing vectors

→ Oiled papers /flypaper (= a long strip of sticky paper hung in a room to catch flies or other insects)

→ Traps of ultraviolet light (culicoides)



Controlling the vectors

Sanitization methods

→ Risk identification

→ Monitoring and surveillance of vectors

→ Trapping systems for capturing vectors

→ Dragging/flagging (for ticks)

→ This method is based on passing a 1-m^2 white tissue over the vegetation and checking the tissue for the presence of caught ticks every 5–10 m.

Controlling the vectors

Sanitization methods

→ Risk identification
→ Monitoring and surveillance of vectors

→ Trapping systems for capturing vectors

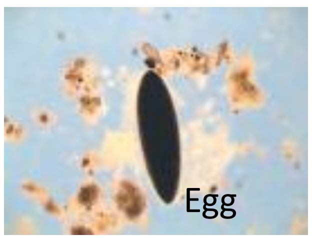
→ Tsetse fly traps (non-return device)

→ Biconical blue and black trap (Challier-Laveissière system)
→ Blue color (external): attractive
→ Black color (internal): stimulates landing
→ Attractive odors:
→ Acetone, octenol, ruminant urine

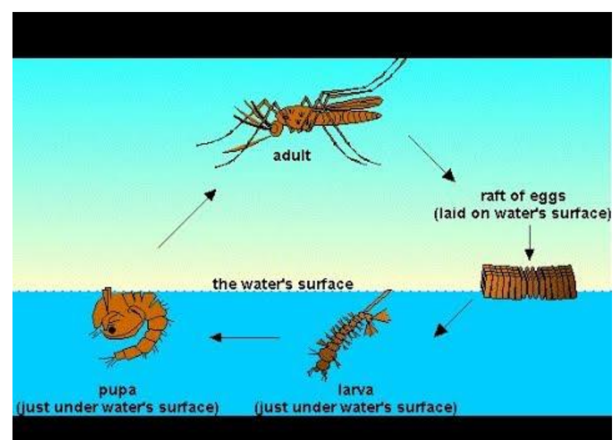
Controlling the vectors

Sanitization methods

→ Risk identification
  → Monitoring and survey of vectors
  → Vector survey : example of mosquitoes
    → Collecting and identifying aquatic larvae and nymphs of mosquitoes
      → Possibility to control vector populations



Diagnostic:
- Eggs: -
- Larvae : +++
- Nymphs: -
- Adults: +++



Controlling the vectors

Sanitization methods

→ Risk identification

- → Monitoring and survey of vectors
- → Vector survey : example of mosquitoes

- → Lifetime of a mosquito
  - → In laboratory (optimized life conditions): 8 to 10 months
  - → In the field
    - → Limitations by enemies
      - → Predators: birds, bats, others arthropods
      - → Pathogens: protists, fungi, viruses
    - → 10% mosquitoes have a lifetime > 10 days
    - → Few of them survive more than 1 month

Controlling the vectors

Sanitization methods

→ Risk identification
  → Monitoring and survey of vectors

Figure 2

→ Development of mosquitoes
  → 8-10 days as a function of species and temperature

  → As a function of soil nature, rainfall patterns, temperature, altitude, natural vegetation

  → Easy adaptation in urban areas

→ Mosquito breeding grounds
  → Stagnant water areas, not too cold

→ Female anophele lifetime
  → About 30 days between 20 and 30° C

Controlling the vectors

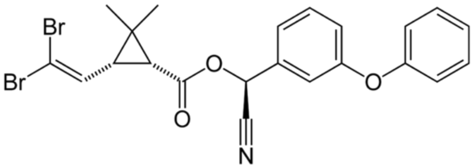
Physical methods

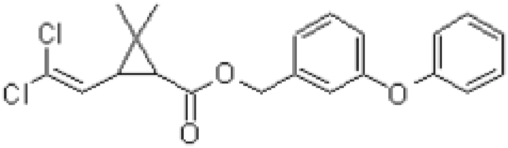
→ Aim: Diminution of human-vector contacts

Insecticide-treated bed net

→Pyrethroids:

Deltamethrin or permethrin





Washing- and cleaning-resistant textile

→ Resistant to about 50 washes

→Impregnated uniforms

→Anti-insect grids on windows and doors

Controlling the vectors

Physical methods

→ Aim: Reduction of human-vector contacts

→ Light traps (UV), electric grids releasing octenol, sticky bands + attracting food or pheromones

→ Against tsetse flies and Tabanidae

→ Catching from 1 to 2 kg tsetse flies

Controlling the vectors

Ecological methods

→ Aim:

→ Create adverse environmental conditions for vector/intermediate host development

→ Health education and population participation are essential

Examples:

- Drain swampy areas (against mosquitoes and molluscs)
- Clear river banks (against black flies)
- Dry irrigated areas (against mosquitoes)
- Maintenance of canal irrigiation (against molluscs)
- Pasture rotation (against ticks)
- Remove aquatic plants (against fluke)
- Improve housing (against Reduviid bugs)

Controlling the vectors

Ecological methods

→ Aim: Reduction of human-vector contacts

Enabling environment → creating adverse conditions for vector/intermediate host survival and outbreak

Other examples:

- Choose adapted home water storage → unfavorable for mosquito development
- Introduce fresh water turtles
  → eat mosquitoe larvae
- Remove abandoned containers or cover them (against mosquitoes)
- Ensure efficient waste pickup → limiting rat populations (leptospirosis), small rodents (leishmaniases)
- Install latrines → adapted to control mosquito development (against *Aedes aegypti* / styrofoam balls → preventing egg laying)
- Remove leafy plants and clogg hollows of trees (against mosquitoes)
- Maintenance of rainwater and wastewater evacuation systems
- Intra-housing control: container of black colour + water + Teepol (surfactant) → larvicidal effect

Controlling the vectors

Chemical methods

→ Aim: Use of natural or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

  - Before 1940 :

  – **Compounds of mineral origin** : derivatives of arsenic, sulphur, fluorine and copper

  – **Organic compounds**
    - Synthetic: alkyle thiocyanates
    - Natural origin: nicotine, rotenone, pyrethrum, …

Controlling the vectors

Chemical methods

→ Aim: Use of natural origin or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

- From 1940 to 1960 :

  - **Halogenated organic compounds (organo-chlorine compounds)** :

    - DDT (dichloro-diphenyl-trichloethane)

    → First « modern » insecticide used at the beginning of the second world war

    → Very efficient against :

    → Mosquitoes → vectors of malaria

    → Lice → vectors of typhus (provoked by bacteria → *Rickettsia*)

    → Used in agriculture against insect pests

    → Mechanism of action on insects

    → Opening sodium channels in insect neurons

    → Spasms, then death

    → Resistances as a consequence of genetic mutations

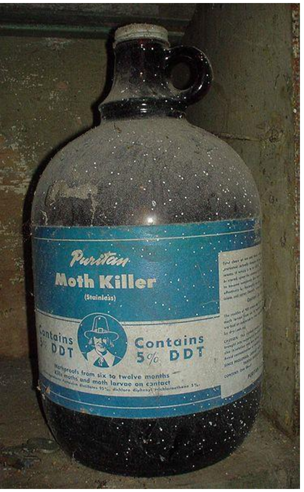
    → Ecological impact

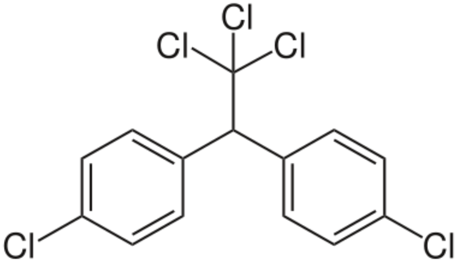
    → Toxicity for birds and fishes

    → Accumulation in the food chain

    → WHO policy : tolerance for indoor use in malaria high-endemic areas

    Discontinuance of DDT was planned for 2020…





→ DDT → contributed to malaria disappearance in Europe and North America at the end of the XIXth century

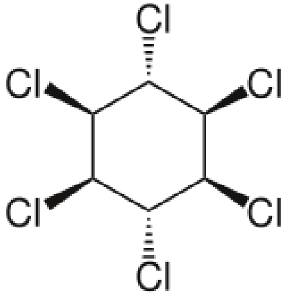
Controlling the vectors

Chemical methods

→ Aim: Use of natural origin or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

- From 1940 to 1960 :
- **Halogenated organic compounds (organo-chlorine compounds)** :



  - HCH (hexachlorocyclohexane) or lindane
    - → Forbidden in France
    - → Prohibition in the world in the near future
    - → Use
      - → Domestic use: against insects
      - → Human treatment against mange (*Sarcoptes scabiei*) and lice
      - → Treatment of cattle against ticks
    - → Mechanism of action
      - → Inhibitor of GABA receptor

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  - Cyclodienes (aldrin, chlordane, heptachlor), chlorinated camphenes (endosulfan) (discontinued: non- or few-biodegradable, toxic)
    - → Mechanism of action :
      - → Cyclodienes : inhibitors of GABA receptors

Controlling the vectors

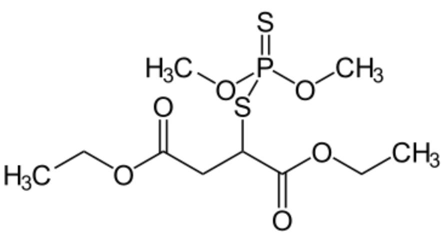
Chemical methods

→ Aim: Use of natural origin or synthetic substances having insecticide activity

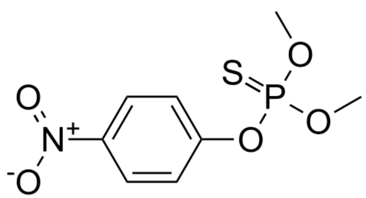
- Diversity of compounds and ecological impact
- From 1960 :

  - **Organophosphorus compounds**

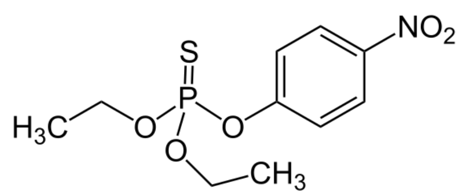
  → Contact insecticides → less stable → less persistent



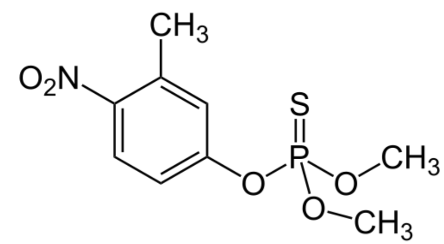
Malathion



Parathion-methyl



Parathion-ethyl



Fenitrothion

→ Mechanism of action : acetylcholinesterase inhibitors

Controlling the vectors

Chemical methods

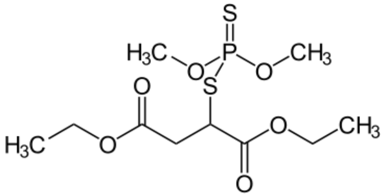
→ Aim: Use of natural origin or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

- From 1960 :
  - **Organophosphorus compounds**

- Malathion → Forbidden in France since 2008

→ Insecticide and acaricide



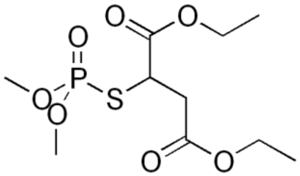
→ Very toxic for bees

→ Application on water areas → Decrease of amphibian populations

→ In 1999, in New-York → Treatments sprayed from airplanes to eradicate West Nile virus

→ Human toxicity: low but, degradation product, malaoxon: very toxic

Malaoxon



- Parathion → Forbidden in Europe and France since 2001

→ ½ life of degradation in soil: 14 days

→ « Dirty dozen » : one of the 12 major toxic components worldwide

Controlling the vectors

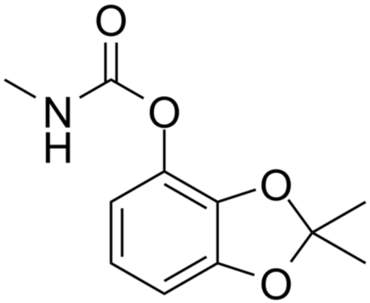
Chemical methods

→ Aim: Use of natural origin or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

- From 1960 :

- **Carbamates** (carbaryl, proposan, carbosulfan, propoxur, bendiocarbe, dioxacarbe)
  - → Insecticides, fungicides, herbicides
  - → Against mosquitoes: propoxur, bendiocarbe, dioxacarbe
  - → Long persistence
  - → Mechanism of action : acetylcholinesterase inhibitor



Bendiocarbe

→ Compounds withdrawn from the market in France on 2007 because of toxicity

Controlling the vectors

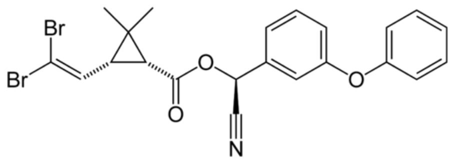
Chemical methods

→ Aim: Use of natural origin or synthetic substances having insecticide activity

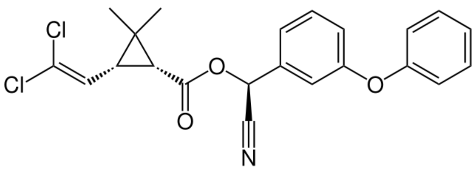
- Diversity of compounds and ecological impact

- **Pyrethroids**

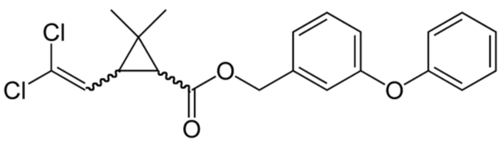
Deltamethrin



Cypermethrin



Permethrin



→ Pyrethrum derivatives

→ Low toxicity for warm-blooded animals by contact or ingestion

→ Highly toxic for bees and fishes

→ Highly biodegradable → almost non-existent persistence

→ Mechanism of action :

= those of DDT : sodium channel inhibitors

Controlling the vectors
Chemical methods

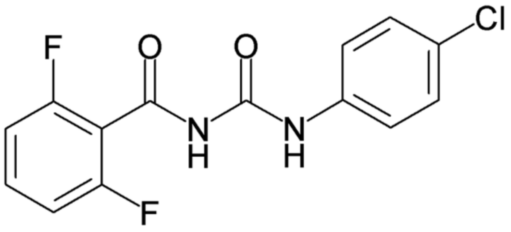
→ Aim: Use of natural origin or synthetic substances having insecticide activity

- Diversity of compounds and ecological impact

- Benzoyl urea derivatives

→ Insecticide class discovered on 1972

→ Diflubenzuron:



→ Mechanism of action: Chitin-synthetase inhibitor

→ Impairment of cuticular structure

→ Insect death during the next moulting

Controlling the vectors

Chemical methods → Bio-rationale methods

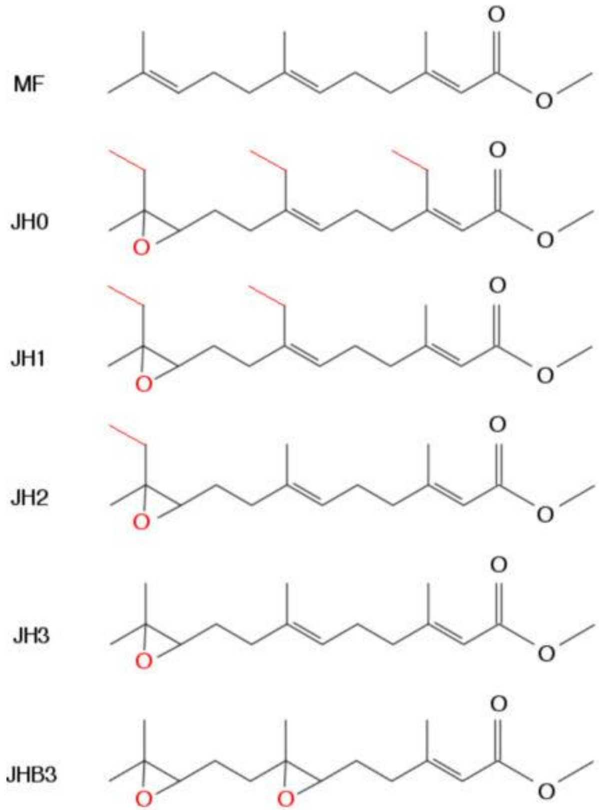
- Word « bio-rationnel » : appeared on 1974

  → Insecticide approach based on the insect physiological knowledge and respectful of the environment

- Hormonal approach

  - Juvenile hormone analogues (JH)

    → Sesquiterpenoids from Methyl-farnesoate (MF)



Controlling the vectors

Chemical methods → Bio-rationale methods

- Hormonal approach
  - Juvenile hormone (JH)

→ Allows larva growth but inhibits differenciation into adult through maintaining the larval stage

→ In adult stage → JH regulates reproduction (vitellogenesis, ovogenesis)

→ JH concentration should be almost nonexistent to get the adult stage

→ JH: not stable enough to be used as insecticide

→ Application of JH-like or juvenoid products

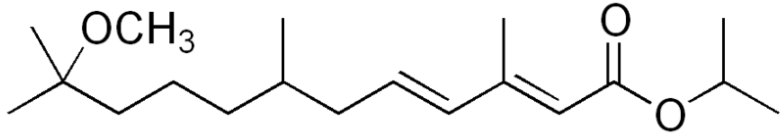
→ Irreversible morphological alterations

→ Insect death

Controlling the vectors

Chemical methods → Bio-rationale methods

- Hormonal approach



- Methoprene

→ Racemic mixture of R,S-methoprene marketed as Altosid® in 1975

→ Active principal: S-methoprene

R-methoprene: inert compound

→ Not toxic for mammals

→ Inactive on insect adult stage

→ Mechanism of action

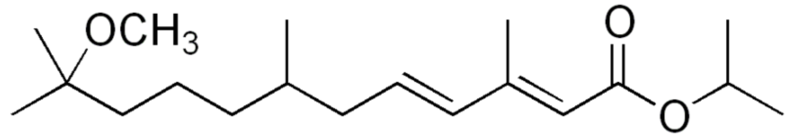
→ Growth regulator

→ JH mimetic

Controlling the vectors
Chemical methods → Bio-rationale methods

- Hormonal approach

  - Methoprene



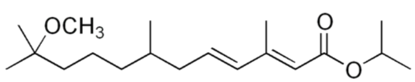
  - Methoprene use

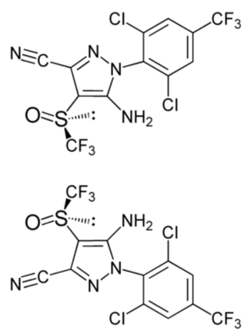
    → Agricultural sector → against insect pests of food

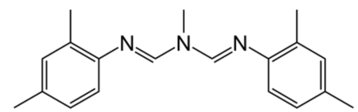
    → Against fleas

In 2011

S-methoprene + fipronil + amitraz = Certifect® (Merial)





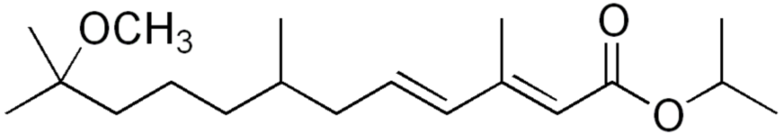


Fipronil → disrupts the insect central nervous system by blocking the ligand-gated ion channel of GABA A receptor and glutamate-gated chloride (GluCl) channels

Amitraz →behavioral changes in both argasid and ixodid ticks, often manifested as hyperactivity, leg shaking and detaching behavior Behavioral effects → secondary to the actions of amitraz on tick octopaminergic G protein-coupled receptors (GPCR)

→ Action against fleas and ticks

Controlling the vectors
Chemical methods → Bio-rationale methods



- Hormonal approach

  - Methoprene use

  → Control of mosquitoes
    → Present formulations only contain S-enantiomer
    → Inhibits adult emergence
    → Genera *Anopheles* and *Aedes* are more susceptible to methoprene than *Culex*
    → Application technique: spraying (vaporization)
    → Low persistence: 24 h outside
    → Need of encapsulation
      → ½ life = 4 to 7 days in summer conditions (T°C max and maximum sunshine)

    → Methoprene → active on populations resistant to usual insecticides
    → Formulation recently released: biodegradable briquets (Altosid®)
      → Allow the management of mosquitoe populations during successive floods

Altosid®

Controlling the vectors
Chemical methods

- Xenobiotics metabolization

  - Metabolization pathways:

  → Metabolic activation

  → Ex.: Parathion (pro-insecticide)

  → Metabolized in less toxic compounds

  → Ex.: Pyrethrinoids

  → Transformation of liposoluble compounds into hydrosoluble derivatives (hydroxylated compounds, glycoconjugates)

  → Acceleration of their excretion in aqueous media

  - Enzyme systems involved :

  Enzyme systems successively get in place during an intoxication

  - Phase I enzymes (functionalization):

  → Catalyzing oxidation, reduction, and hydrolysis reactions

  → Add or unmask electrophilic or nucleophilic chemical groups of the xenobiotics

  - Phase II enzymes (conjugation):

  → Fixation of hydrophilic endogous compounds (glutathione, glycuronic acid, glucoside, sulfates or phosphates) on functional chemical groups obtained from phase I

Controlling the vectors
Chemical methods

- Resistance to insecticides

- Causes

    - Intensive use of insecticides in agriculture

        → Preventive or curative

        → Massive use

            → Purpose : eradication

                → Selection of organochlorine-resistant insects (*Anopheles*, *Culex*, *Aedes*)

- Consequences

→ Lower susceptibility to insecticides during disinsecting campaigns to control vector populations

→ Necessity to increase the doses (x 10, x 100, x 1000)

→ Overcost, toxicity also due to product remanence

→ Increase of human diseases transmitted by mosquitoes

Controlling the vectors
Chemical methods

- Resistance to insecticides

- Insecticide resistance mechanisms
  - Effect on insecticide target
    - Modification of molecular target of insecticides
      → decrease or disappearance of the insecticide-target association
    - Inactivation of the insecticide

    - Alleles of resistance genes involved in:
      - the insect behaviour (insecticide avoidance)
      - one of the pathways involved in target production
        → pre-exist in the mosquitoe population
        → or appear through mutation :
          - point mutations
          - chromosomal rearrangements

  - Causes of resistance
    - The selective pressure
      → promotes the selection of mosquitoes with these alleles within a genetically heterogeneous population

      → their proportion increases within the population from one generation to the other
        → Mosquitoes homozygote for the gene of resistance

Controlling the vectors
Chemical methods

- Resistance to insecticides

- Insecticide resistance mechanisms

- Parameters regulating resistance dissemination within a population
    - Level of dominance / recessivity
    - Selective advantage ?
    - Frequence of mutations
    - Speed of generations
    - Fertility rate
    - Chromosomal or extrachromosomal localization of resistance genes

- Several resistance mechanisms can together appear in one population
    → Rates of insecticide resistance increase

- When a resistance is acquired against one insecticide
    → Usually provokes resistance to another one
        → Cross resistance

Controlling the vectors
Chemical methods

- Consequences of the chemical product use

- Insecticides have several deleterious effects on the environment:

- Ecological imbalance :
  - Modification of predator-prey balance
- Groundwater pollution :
  - Because of their remanence
- Accumulation in trophic chains
  - Contamination of food → human health concern
- Toxicity for insecticide user

Controlling the vectors
Chemical methods

- Developing a reasoned approach

  - Aims of a reasoned control

    → Reducing insecticide quantities
    → Reducing food pollution
    → Reducing resistance emergence

- Need for an in-depth knowledge on

  - The population dynamics through trapping and breeding
  - An appreciation of the damaging level of insects
  - Survey of insecticide susceptibility in vectors

- Reasoned control → supported by national and European regulations with the aim to reduce the pesticide use by 30 – 50% on the next ten years

→ Marketing new insecticides → more and more difficult

  - Time for product development : 15 years

Controlling the vectors
Biological methods

- Aim: Reducing vector populations causing damages through the use of living organisms or their products

→ Method: generate and maintain an ecological imbalance

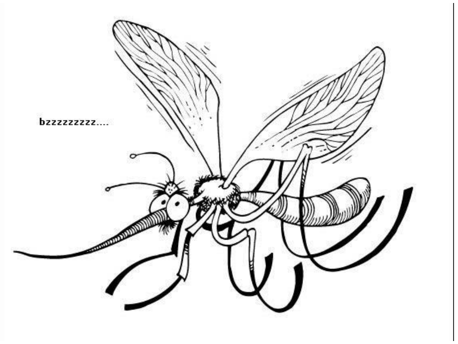
- Historical data
  - The oldest known method: 304 before Christ in China: use of ants against a lemon tree beetle (the coleoptera: *Clitea metallica*)

  - 1889 in California :

Use of the Australian ladybug *Novius cardinalis*, as predator of the Citrus fruits cochineal, *Icerya purchasi*.

Controlling the vectors
Biological methods

- Identification of natural auxiliary living organisms



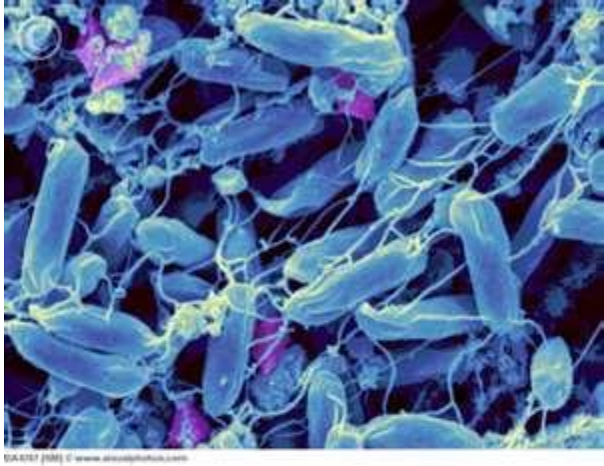
- Types of natural auxiliary living organisms
  – Predators : kill their preys to eat them
  – Parasitoids : are dependent on their host and kill them
  – Parasites : are dependent on their host

- Development of protection means of natural auxiliary living organisms

– Need of a reasoned chemical control

Controlling the vectors
Biological methods

- Introduction of entomopathogens



Action: they can directly act or through toxins they generate

– Entomopathogenic bacteria
  - *Bacillus thuringiensis* (B. t.) : Gram-positive, aerobe or facultative anaerobe, spore-forming rod shaped bacterium
  - Identified in *Bombyx mori*.
    - B.t. synthezises and excrete protein crystals → toxic for some insects

→ Insecticide effect on lepidoptera, coleoptera, diptera

→ Destruction of midgut cells of the insect larva

→ Death of the insect larvae that can be consumed by the bacteria

- Applications:

→ From 1933

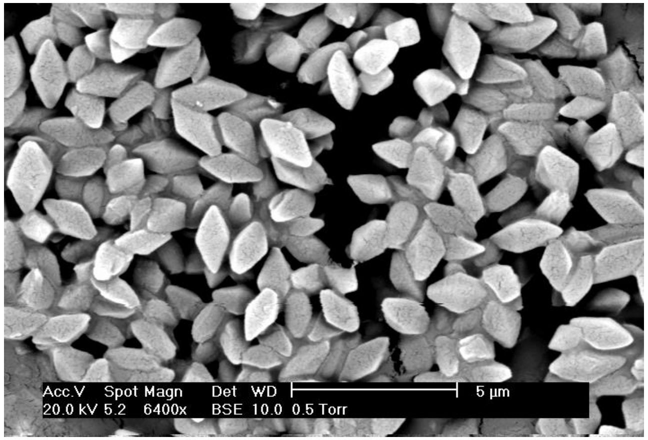
→ 1950-1970: Eradication of lepidoptera in forest, fields crops, vineyards

→ 1976: Discovery of the « israelensis » Bti serotype

→ Larvicidal actions on mosquitoes, blackflies, coleoptera

Controlling the vectors
Biological methods

- Introduction of entomopathogens



– Entomopathogenic bacteria

- Bt toxins → Very sensitive to UV
  → Low remanence on the leaves
  → Higher residual action in soil
  → Biotechnologies: transgenic plants producing Bt toxins
  → Issue of toxin degradation in soil…
  → Permitted in organic agriculture

- Toxin molecular weights → vary as a function of the strains
  → Impact on the spectrum of activity:
  → Some strains → more active against lepidoptera, and/or diptera, coleoptera
  Example : B.t. var. *israelensis* → mosquitoes

- New strains produced by genetic engineering
  → 14 genes isolated encoding for toxins

- But resistances → alteration of the receptor affinity site for the toxin → reduction of the toxin binding to intestinal cells

- *Bacillus sphaericus* : used against *Culex quinquefasciatus* (urban tropical areas)
  - Spores ingested by insect larvae → active bacteria → lethal toxines

Controlling the vectors
Biological methods

- Introduction of entomopathogens

– Entomopathogenic bacteria

  - Conditions required for the insect death after Bti treatment
    - → Catching and ingesting a Bti crystal
    - → Having a highly alkaline digestive tract
    - → Having enzymes able to transform protoxins in toxic compounds
    - → Having adequate and functional membrane receptors

  - Safe for human and pets

Controlling the vectors
Biological methods

- Introduction of entomopathogens

  - Entomopathogenic bacteria

- Marketed formulation: VectoBac®

  - Biological larvicide

    → Highly specific against all kinds of mosquitoes

    → Used as dispersible granules

    → Active principle

      → *Bacillus thuringiensis* serotype h14

    → Targets: adult and larvae mosquitoes

    → Areas of use: permanently or temporary stagnant water (lakes, ponds, lagoons, wells, swimming pools, septic tanks, ….)

    → Action: quick on larvae

    → Application:

      → Huge surfaces by using agricultural machinary or helicopter/plan

        → Dose: VectoBac® dose: 1kg/ha

      → Small surfaces : Application with a pressure sprayer

        → Dilution: 10 g de VectoBac® WG in 5 liters of water → 100 m^2 breeding site

    → Main advantage: no risk for the natural predators present in the breeding site

Controlling the vectors
Biological methods

- Introduction of entomopathogens
    - Entomopathogenic bacteria

        - Marketed formulation: VectoLex®

- Biological larvicide

→ Biological larvicide containing *Bacillus sphaericus*

→ Highly specific against all kinds of mosquitoes, used since 2005

→ Used as corn-based granules

→ Mosquitoe larvae

→ Ingest bacteria

→ Toxins released in the larva midgut

→ Paralysis then death

→ Dead larvae at the air-water interface

→ Toxins released → ingested by other larvae

→ VectoLex® → Larvae control for 6 weeks

Controlling the vectors
Biological methods

Introduction of entomophage fishes

- As soon as 1920, observations in USA and Mexico

→ Mosquitofish (*Gambusia holbrooki* and *Gambusia affinis*)

→ Species of freshwater fish (*Poecilidae* family)

→ feeds on mosquitoe larvae

→ Small fish:

Male: 3-4 cm; female 8 cm

→ Prefers stagnant water

→ Accomodates to running water

→ Slightly resistant to insecticides

Controlling the vectors
Biological methods

Introduction of entomophagist fishes

Operational use of mosquitofishes

→ High capacity of larvae consumption
  → One single mosquitofish
    → consumes one hundred larvae or nymphs a day

→ Ability to control their own regulation by eating their youngs when space is reduced
  → Do not overpopulate an area

→ Easy breeding and transport:
  → Put young fishes in an empty stomach 24 h for transport

Controlling the vectors
Biological methods

Introduction of entomophagist fishes

Operational use of mosquitofishes

Some examples of larvae control

→ Algeria: larval control of anopheles is some oases
→ Iran: 3000 rivers and accumulations of stagnant water
  → 1969: 1.5 million mosquitofishes were released
    → Reduction of malaria in Southern Iran
→ Afghanistan: 6 million mosquitoefishes released on 1971

Results

- Positive concerning the control of mosquitoe populations
- Difficult to evaluate the epidemiological effects because concomitant improvement of the antimalarial chemoprophylaxis

Controlling the vectors
Biological methods

Introduction of entomophagist fishes

- The main problem of the tropical larval habitats
  → Seasonal drainage (rice fields, temporary waterways, irrigated grasslands)
  → *Gambusia affinis*: not able to survive in dry areas

- Other larvivorous fishes

  → *Nothobranchius guentheri* (Tanzania)
    → size: 5-7 cm

  → *Cynaolebias bellortii* (Argentina, Brazil)
  → Can survive with eggs buried in the ground
  → Able to adapt to various habitats and temperatures

→ Studies are currently running in Africa

Controlling the vectors
Biological methods

Introduction of entomophagist fishes

- Limitations to the use of larvivorous fishes

- Prefered areas by *Anopheles gambiae*, the main vector of Human malaria
  → small temporary stagnant water areas
    → not adapted to *Gambusia* fishes

- Larvivorous fishes
  → voracious
  → necessary to verify that young fishes are not preys of larvivorous fishes

→ Just an additional mean to control insect vectors

Controlling the vectors
Biological methods

- Autocidal methods

- Introduction of males having particular characteristics
  - → Approach used against several insects (mosquitoes, flies)
  - → Breeding of males in a great quantities
    - → Sterilized using irradiation
      - → Released in the wild (minimum 10^3 to 5×10^3 /km^2)

Example : Sterile males by using gamma irradiation

- → Screwworm (*Cochliomya hominivorax*) in USA
  - → Myiasis → cattle/Human (abscess and weakening)
  - → Females lay eggs in the wounds of cattle, but <u>they do not hatch</u>
    - → Reversing the spread in USA in 1982
    - → Control program in Mexico, Nicaragua, Costa-Rica, Jamaica

Controlling the vectors
Biological methods

- Control by transgenesis

- Principle

→ Use of trangenic males exhibiting specific genetic characteristics leading to:

→ sterility

→ death of progeny

→ sex-ratio in favour of males

→ annihilated vectorial capacity

- Under investigation

→ Transgenic mosquitoes unable to transmit malaria, dengue fever, …

→ Sandflies unable to transmit leishmaniases

→ Tse-tse flies unable to transmit African trypanosomiasis

→ Transgenic mollusks unable to transmit schistosomiasis

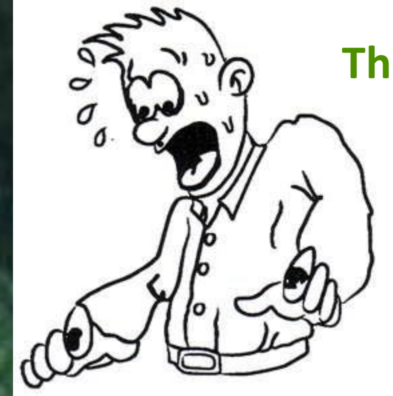
- Challenges

→ Need to identify genes involved in vectorial capacity

→ Insert mutated genes at the right place into the genome with successful expression

→ Get transgenic vectors able to replace natural vectors

→ Parasites can adapt to the modified genes?



Thank you for your attention !