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Presented by:

Dr HAKIMI Sakina (Assistant Professor)

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Introduction

In recent years, there has been a notable resurgence of infectious diseases of various types, particularly vector-borne diseases, while new diseases have also emerged (such as Rift Valley fever and West Nile fever). A major concern has arisen due to the re-emergence of parasites and viruses that had previously been under effective control in certain regions of the world, including malaria, leishmaniasis, Japanese encephalitis, yellow fever, and dengue fever. Furthermore, the geographic range of arthropod vectors transmitting these diseases has continuously expanded, exposing new human populations to the risk of infection.

Whether they are insects or mites, disease vectors actively transmit pathogens from an infected vertebrate host to another host, causing parasitic diseases (such as malaria), bacterial diseases (such as Lyme disease), and viral diseases (such as dengue fever, chikungunya, Zika, and others) among humans. These diseases may be exclusively human or may be transmitted between animals and humans (zoonotic diseases). Transmission of vector-borne diseases most commonly occurs through bites, but may also occur through the feces or even regurgitation of the vector insect.

Vector control has proven to have a significant impact on the prevention and management of vector-borne diseases. Environmental conditions favorable to disease vectors play a major role in determining the geographical distribution and incidence of these diseases. Knowledge and understanding of these characteristics provide a unique opportunity for preventing and controlling such diseases by reducing human-vector contact, decreasing vector density, and eliminating conditions that support vector survival.

1. Climate Change and the Emergence of Vector-Borne Diseases in Humans

Climate change significantly affects pathogens (parasites, viruses, and bacteria), vectors, and reservoir hosts, thereby influencing and increasing the transmission of many diseases. Many vectors are currently expanding into higher latitudes and altitudes, while the duration of their seasonal activity is increasing. These trends are expected to continue as global temperatures rise.

Vector systems consist of three essential components: the infectious agent, the vertebrate host/reservoir, and the vector. The effects of climate change are likely to be most evident at the intersections of these three components. Climate change, particularly global warming, is considered a major factor in altering the epidemiological landscape. Increased warming and drought in tropical regions may severely affect arthropod vector populations.

In a report published in 2017, the World Health Organization (WHO) alerted governments to the need for action regarding the risk of disease exposure among global populations, which varies according to geographic and climatic zones. Today, more than 80% of the world's population lives in areas at risk of diseases such as malaria, Lyme disease, dengue fever, chikungunya, or Zika.

Vector control, which includes the management of insects, ticks, freshwater snails, and rodents that transmit parasites, bacteria, and viruses, is a topic of great importance in primary healthcare and public health. This issue is particularly significant in Africa due to its high biodiversity, which has resulted in abundant and diverse biological resources arising from geographic, soil, and climatic diversity, in addition to demographic factors, poverty, and other socio-economic conditions.

Deficiencies in environmental sanitation and environmental health services, combined with overcrowded living conditions in both urban and rural communities, contribute to the proliferation of disease vectors, particularly mosquitoes, bedbugs, cockroaches, and rats. This increases the likelihood of disease transmission while also causing nuisance and economic losses. Given the threat vectors pose to public health and the potential risks associated with the improper use of pesticides, it is essential that vector and rodent control measures be effective, safe, and environmentally sound. Consequently, emphasis should be placed on environmental management methods that reduce breeding and sheltering sites for insects and rodents, thereby lowering their populations. Chemical pesticides should be used only when necessary. This principle constitutes one of the foundations of Integrated Vector Management (IVM), which is implemented by many countries worldwide and recommended by the World Health Organization.

2. Disease Vectors

Disease vectors are living organisms that transmit pathogens and parasites from infected individuals to healthy individuals, resulting in serious diseases affecting both humans and animals. In addition to causing premature mortality and disability, they represent a substantial obstacle to economic development because of lost working hours, high healthcare costs, and expenditures associated with vector control.

These vectors mainly include blood-feeding insects and ticks (hematophagous arthropods) that ingest pathogens while taking a blood meal from an infected or infested host and subsequently transmit them to a healthy host.

Vector-borne diseases are particularly prevalent in tropical and subtropical regions where access to safe drinking water and sanitation systems is limited. These diseases account for approximately 17% of the estimated global burden of all infectious diseases. Malaria remains the deadliest vector-borne disease, whereas dengue fever is the most rapidly spreading.

3. Definition of Control

Control refers to the reduction of damage caused by a pest through its exclusion, prevention of contact with the host, elimination, or the creation of unfavorable conditions for its reproduction. Applied control methods are those implemented by humans with the aim of reducing harm to people or property. These include chemical control, biological control, physiological control, and integrated control.

Integrated Pest Management (IPM) is considered the most effective approach because it is based on maximizing the use of mechanical, biological, and physiological control methods while resorting to chemical control only in extreme situations or when other methods fail. Prevention, public awareness, and adherence to guidelines and recommendations also play a crucial role in controlling public health pests.

Compliance with the recommendations of the World Health Organization is equally important. WHO is a specialized agency that supports the development of health systems worldwide and promotes environmental health protection. Disease prevention is one of its primary objectives, alongside curative and preventive healthcare services.

Vector control is a fundamental component of disease prevention. It includes surveillance and protection against vectors of human pathogens, such as mosquitoes and rodents. Control measures encompass chemical and biological methods, environmental interventions, health education, community mobilization, and the continuous evaluation of all these approaches. The objectives are to reduce the risks of disease endemicity and epidemics, limit pathogen transmission through vectors, and manage outbreaks of vector-borne diseases.

It is noteworthy that among the 22 vector-borne diseases identified by the World Health Organization, Algeria has selected those that pose a significant threat due to its extensive borders, particularly arthropod-borne viral diseases. Preventive measures have been adopted to address these threats while carefully adhering to WHO recommendations.

In Algeria, the World Health Organization promotes Integrated Vector Management as the most effective strategy for strengthening vector control efforts. Since the health sector alone cannot prevent the spread of vectors and vector-borne diseases, other sectors such as environment, agriculture, and local administrations are encouraged to contribute. Given Algeria's geographical, social, and economic characteristics, as well as its environmental and climatic conditions, coordinated action is essential. This requires an integrated, systematic, proactive, multidisciplinary, and institutional approach involving all sectors and stakeholders, reflecting the national slogan:

"Vector-borne diseases: everyone is concerned."

4. The Danger of Vector-Borne Diseases

Vector-borne diseases are among the most dangerous and unpredictable diseases. Their prevention and control are particularly challenging because infections may reappear even after treatment, and the organisms involved are often deeply established within the environments where they occur.

The danger of vectors lies in their ability to spread diseases more rapidly and over a wider geographical area than diseases requiring direct human-to-human transmission. Moreover, vectors can transmit pathogens from various animal species—including rats, mice, monkeys, birds, dogs, and others—to humans. They facilitate the spread of numerous microorganisms

responsible for severe diseases. Treatment of these diseases is often difficult, and effective protection largely depends on eliminating or controlling the vector itself.

. 5. Criteria for Vector Control

A disease vector is an animal that carries pathogens, which are among the leading causes of illness and death in many disaster situations. Vector-borne diseases can be prevented and controlled through various interventions, including appropriate site selection, provision of adequate shelter, ensuring sufficient water supplies, proper disposal of organic waste, effective solid waste management and sanitation systems, and the delivery of healthcare services. Chemical pesticides should be considered only as a final measure when necessary.

Although vector-borne diseases are often complex in nature and may require consultation with specialists to address associated challenges, many simple and practical control measures can be implemented once the disease, the vector, and its relationship with the affected population have been identified.

6. Technical and Administrative Challenges Facing Vector Control

Vector control currently faces a variety of challenges, including resistance to drugs and insecticides, increased vulnerability among marginalized populations (such as rural communities, the urban poor, and displaced persons), global environmental changes, and local environmental modifications resulting from development projects, changes in hydrology, and land-use practices. Additional challenges include increasing competition for limited health resources.

Large-scale vector control campaigns are often difficult to implement because of financial constraints, operational difficulties, and potential adverse impacts. For these reasons, attention has increasingly shifted toward alternative approaches that individuals and communities can apply for their own protection. These approaches are generally less dependent on large government-led control programs and place greater emphasis on community participation.

Furthermore, many traditional preventive methods are no longer as effective as they once were, leading to the re-emergence of diseases in new environments or to the resurgence of diseases in more virulent forms. At the same time, numerous pathogens have developed resistance to commonly used medications, while many vectors have acquired resistance to insecticides.

Consequently, vector control programs must be coordinated across all relevant sectors, national capacities must be strengthened and adapted to emerging needs, and control strategies should be implemented within the framework of an integrated management approach. Such an approach promotes collaboration among public health, environmental, agricultural, and local governance sectors to ensure sustainable and effective vector control and disease prevention.

I-Prophylaxis and Prevention of Vector-Borne Diseases

Vector-borne diseases, transmitted by arthropods such as mosquitoes, ticks, and fleas, constitute a major global public health threat and are responsible for more than 700,000 deaths annually. Therefore, control strategies must incorporate effective vector management programs, with a strong emphasis on disease prevention and control. Many researchers are currently warning public authorities about the potential spread of vector-borne diseases that were once confined to tropical regions. As global temperatures continue to rise, the geographical distribution of mosquitoes transmitting malaria, chikungunya, dengue fever, and Zika virus is expected to expand over the coming decades, making the implementation of preventive measures increasingly important.

1. Prophylaxis and Prevention

Prophylaxis, or disease prevention, refers to a set of preventive measures and actions designed to prevent the occurrence and spread of diseases or pests. It involves the application of effective methods and strategies aimed at preventing disease, reducing the risk of infection, or limiting its impact. Prevention is therefore based on comprehensive protection through the implementation of various preventive measures intended to reduce the emergence and progression of diseases.

It also includes identifying and analyzing all issues related to a disease and its vectors in order to develop effective, sustainable, and appropriate control techniques according to the nature and abundance of the vector. Prophylaxis encompasses sanitation, disinfection, hygiene, precautionary measures, and protective interventions.

More broadly, prevention refers to active or passive processes intended to prevent the onset or spread of disease. It includes both medicinal interventions and preventive awareness campaigns, as well as the adoption of best health practices. Individuals exposed to a potential health risk may initiate preventive measures before disease develops. Prevention is not, in itself, medical treatment, although it may lead to therapeutic intervention. Rather, it links awareness of actual or suspected risks with appropriate medical or public health responses.

2. Types of Prevention

-Primary Prevention

Primary prevention aims to prevent the occurrence of disease in healthy individuals. It includes measures designed to reduce the incidence of diseases or health problems within a population by eliminating or minimizing their causes and risk factors. The term "incidence" refers to the occurrence of new cases within a population.

-Secondary Prevention

Secondary prevention aims to prevent disease progression or recurrence through early detection and prompt treatment. It involves identifying diseases or health problems at an early stage and implementing rapid and effective interventions to reduce their harmful consequences.

-Tertiary Prevention

Tertiary prevention consists of measures intended to reduce the severity of existing diseases and prevent complications. These measures aim to minimize disabilities, impairments, and suffering while improving quality of life. Tertiary prevention is therefore a major component of medical care and rehabilitation programs.

3. Preventive Measures

At the community level, vector control techniques are implemented to reduce vector populations or decrease human exposure to them. Surveillance of vector-borne diseases represents a major public health priority. Alongside effective control strategies and awareness campaigns, vector management remains one of the most appropriate responses for protecting populations most vulnerable to these diseases.

Several preventive approaches can reduce the risk of vector-borne infections, including:

- **Chemical protection**, through the use of skin-applied insect repellents or insecticide-treated clothing.
- **Mechanical protection**, such as wearing long-sleeved clothing and long trousers.
- **Chemoprophylaxis**, particularly against malaria.
- **Vaccination**, for diseases such as tick-borne encephalitis and dengue fever.
- **Environmental management**, aimed at reducing vector breeding habitats.

Public health campaigns also play a vital role in educating communities about disease prevention strategies, promoting hygienic practices, and encouraging participation in vector control programs. These initiatives help improve awareness and increase adherence to preventive measures.

4. Preventive Measures Against Vector-Borne Diseases

Disease prevention relies on a wide range of available tools, including public information campaigns, hygiene measures, rehabilitation services, immunization programs, early detection, and quarantine procedures. It is based on both primary prevention, which focuses on preventing disease occurrence, and secondary prevention, which addresses disease recurrence and promotes health education.

Prophylaxis can be divided into two major categories:

-Health Prophylaxis (Sanitary Prophylaxis)

Health prophylaxis relies primarily on hygiene and sanitation measures, including:

- Disinfection procedures.
- Establishment of sanitary exclusion zones.
- Quarantine of individuals exposed to infection.
- Screening for latent or incubating infections.
- Identification of carriers and reservoirs of disease.
- Elimination or treatment of infectious animal cases.

-Medical Prophylaxis (Chemoprophylaxis)

Medical prophylaxis involves the use of pharmaceutical and biological products, including vaccines, antisera, and preventive medications. Its principal components include:

- Hygiene and health risk management.
- Disease diagnosis in the field or through laboratory testing.
- Treatment using specialized medications.
- Monitoring animal husbandry practices, including feeding, breeding, and housing conditions.

- Continuous veterinary surveillance through regular inspections and rapid intervention during outbreaks.

4.1 Personal Protection

Personal protection comprises preventive measures designed to protect individuals, families, and communities from vector exposure. It also includes interventions that prevent insects from entering homes and shelters through simple and long-lasting methods such as repellents, protective clothing, mosquito nets, and fine-mesh screens.

The primary objective is to reduce or prevent human and animal exposure to vectors, particularly during periods of peak activity. For example, animal shelters should ideally be enclosed and fitted with screened doors and windows to prevent insect entry. Individuals living in vector-prone areas should wear long-sleeved clothing and cover exposed skin, especially during periods of high vector activity.

Additional personal protection measures include:

-Protection Against Mosquito Bites

- **Use of insect repellents:** Application of repellents to exposed skin is strongly recommended.
- **Protective clothing:** Wearing long sleeves and trousers reduces skin exposure to mosquito bites.
- **Mosquito nets:** Sleeping under bed nets or using screened windows provides a physical barrier against mosquitoes.

-Health Education

Health education programs increase public awareness of vector-borne diseases and encourage preventive behaviors, such as eliminating mosquito breeding sites and using protective measures like mosquito nets.

-Vaccination

Vaccination is a simple, safe, and effective method of protecting individuals from infectious diseases before exposure occurs. Vaccines stimulate the body's natural immune defenses and provide protection against specific infections. Vaccination is particularly important for diseases such as dengue fever and can significantly reduce disease transmission within populations.

Some vaccines are recommended only before travel, for individuals living in high-risk areas, or for people working in occupations associated with increased exposure. Over the decades, vaccination programs have contributed substantially to reducing disease incidence and mortality worldwide.

4.2 Environmental Management in Vector Control

Environmental management is a fundamental component of integrated vector control strategies.

-Water Management

Proper water storage and effective wastewater management help prevent mosquito breeding and are essential for reducing disease transmission.

-Waste Management

The removal of waste materials capable of retaining water reduces mosquito breeding sites and limits the proliferation of other disease vectors.

-Urban Planning

Well-designed urban environments contribute significantly to disease prevention through improved drainage systems, sanitation infrastructure, and environmental management practices that reduce vector habitats.

Environmental management, combined with personal protection, public education, vaccination, surveillance, and integrated vector control strategies, provides a comprehensive and sustainable approach to preventing vector-borne diseases and protecting public health.

.4. 3. Control of Insect Vectors

Effective vector control requires identifying and eliminating insect breeding sites, particularly ponds, marshes, damp areas, and moist organic matter such as animal manure. This can be achieved by properly closing water taps, preventing water leaks, covering damp areas with dry soil, removing animal waste, and regularly replacing bedding materials. Additional preventive measures include draining ponds and marshes, disposing of waste properly, preventing garbage accumulation, securely covering water storage tanks, and eliminating potential water collection sites such as discarded tires, flower pots, and unused equipment.

When leaving a house unoccupied for an extended period, toilet lids, water cistern covers, drainage outlets, and sewer openings should be tightly closed. Water in flower vases should be changed every two days, and containers should be cleaned thoroughly. Standing water in roof gutters and garden drainage channels should also be removed. Animal shelters should be maintained in a clean condition, and drinking water containers for livestock should be cleaned and refilled regularly.

4.4. Repellents

Repellents are among the most widely used methods for preventing insect bites. Traditional repellents include smoke generated from open fires, particularly outdoors. The repellent effect of smoke may be enhanced by burning aromatic wood rich in resins or by using citronella oil applied to the skin or clothing. The duration of effectiveness can be prolonged by mixing these substances with animal fat to reduce evaporation. Other natural repellents include leaves from the neem tree (*Azadirachta indica*).

-Advantages of Repellents

- Easily available.
- Locally known and socially accepted.
- Relatively inexpensive.

-Disadvantages of Repellents

- Short duration of effectiveness.

- Potential discomfort during use due to strong odors or skin irritation.
- Possible side effects in some individuals.

Additional preventive recommendations include:

- Avoid traveling to areas experiencing outbreaks of vector-borne diseases whenever possible.
- Receive recommended vaccinations or preventive medications before travel, such as those against yellow fever or malaria when appropriate.
- Inspect beds, mattresses, and bedding, particularly in hotels, to avoid exposure to bed bugs.
- Avoid swimming in ponds or stagnant water and never defecate in such water bodies.
- Thoroughly dry the skin after water exposure in endemic areas.
- Control snail populations that serve as intermediate hosts of diseases such as schistosomiasis.
- Maintain good personal hygiene, use safe drinking and bathing water, and dispose of human waste away from water sources.

-Flea Control Without Pesticides

Flea infestations can often be managed without pesticide use by:

- Regularly combing pets with flea combs.
- Bathing pets with pesticide-free shampoos.
- Frequently washing pet bedding.

If pesticide treatment becomes necessary, safer topical treatments or oral medications should be considered under veterinary supervision. Consultation with a veterinarian is recommended when selecting appropriate products.

To reduce pesticide exposure:

- Diversify sources of pet food whenever possible.
- Prefer organically grown fruits and vegetables.
- Wash all fruits and vegetables thoroughly before consumption.
- Wash hands frequently, especially before preparing or eating food.

- Clean floors and household surfaces regularly using damp cloths.
- If contact with pesticides occurs, wash exposed skin immediately and remove contaminated clothing before entering living areas.

5. Other Approaches to the Control of Vector-Borne Diseases

Vector control remains an ongoing challenge because both established and emerging diseases continue to pose significant public health threats. More than 80% of the world's population is at risk of vector-borne diseases, and approximately half of these individuals are at risk of exposure to two or more such diseases.

Vector control remains one of the most effective methods for combating many major infectious diseases worldwide. Successful interventions targeting mosquitoes, flies, ticks, bed bugs, and other disease vectors have saved millions of lives and significantly improved public health.

Between 2001 and 2015, two major vector control interventions—namely insecticide-treated bed nets and indoor residual spraying—prevented an estimated 663 million malaria cases in sub-Saharan Africa. Similarly, large-scale vector control programs have substantially reduced the burden of diseases such as onchocerciasis, visceral leishmaniasis, and Chagas disease.

Nevertheless, vector control faces continuing challenges. The emergence of Zika virus outbreaks, the re-emergence of yellow fever, and the increasing incidence of dengue fever and chikungunya have highlighted the importance of sustainable vector control programs and the urgent need to strengthen global preparedness and response capacities.

Given the deterioration of vector control capacities in many regions, there is an increasing need for comprehensive strategies that are effective, locally adapted, and sustainable. Such strategies are not designed to target a single disease but rather to address multiple vectors and diseases simultaneously through multisectoral collaboration involving public health, environmental management, urban planning, education, and other sectors.

This integrated approach enables more cost-effective resource utilization and promotes long-term sustainability of disease control efforts.

5.1. Innovation in Vector Control

Continued investment in innovation is essential. Promising interventions currently under development include:

- New classes of insecticides.
- Spatial repellents.
- Odor-baited traps.
- Improved house screening methods.
- Biological control strategies based on bacteria such as *Wolbachia*.
- Genetically modified mosquitoes.

Once these interventions have been evaluated and endorsed for safety, efficacy, quality, and public health value, they should be incorporated into vector control programs to maximize their benefits.

5.2. Global Strategic Pillars for Vector Control

The global response to vector control identifies four major strategic pillars:

. Strengthening Intersectoral Collaboration

Control of vector-borne diseases is a shared societal responsibility. Collaboration between the health sector and other sectors is essential for effective prevention and control.

. Community Engagement and Mobilization

Active participation of local communities is crucial for ensuring sustainability and trengthening resilience against future disease outbreaks.

. Strengthening Surveillance and Monitoring

Continuous collection and analysis of health and entomological data enable early detection of increases in vector populations and help evaluate whether interventions are achieving their intended outcomes.

. Scaling Up Evidence-Based Interventions

Vector control interventions should be guided by scientific evidence and integrated to maximize disease reduction while minimizing environmental impacts. Data-driven decision-making improves efficiency, sustainability, and public health outcomes.

Together, these pillars form the foundation of modern Integrated Vector Management (IVM), a comprehensive framework that combines environmental management, biological control, chemical interventions, surveillance, community participation, and intersectoral cooperation to reduce the burden of vector-borne diseases worldwide.

II-Chemical Control of Disease Vectors

Vector-borne diseases account for a substantial proportion of the global burden of disease. Their impact extends beyond public health, significantly affecting the economic and social development of affected nations. Mathematical models assessing the economic impact of malaria, for example, indicate that countries where malaria is endemic have average incomes that are only about 33% of those in non-endemic countries. Although many vector-borne diseases are treatable, the high cost of treatment remains a major obstacle for large populations in developing countries.

Malaria continues to have one of the greatest impacts on human health among vector-borne diseases, despite being a preventable and treatable disease. In Africa, malaria has historically caused the death of approximately one child every minute. However, mortality has decreased by more than 50% since 2000, largely due to successful vector control interventions. The World Health Organization estimates that malaria-endemic countries lose approximately 1.3% of their annual economic growth because of the disease. Therefore, prevention through vector control and effective treatment remains essential for protecting populations.

Given the devastating consequences of vector-borne diseases and viral infections, vector control has become a public health priority. In many developing countries, effective vector control programs can substantially reduce mortality rates, particularly among children. Disease transmission is further intensified in these regions by high levels of population mobility.

Vector control constitutes a major component of the current global disease prevention strategy. Numerous documented examples demonstrate that vector control interventions can significantly reduce or even interrupt disease transmission, especially in areas at high risk.

Disease vector control encompasses insects, ticks, freshwater snails, and rodents that transmit parasites, bacteria, and viruses. This field is particularly important in Africa because of its remarkable biodiversity, geographic diversity, varied climatic conditions, and socioeconomic challenges.

Historically, humans have used various substances to protect crops and control pests, including animal manure, ash, clay, lime, and plant extracts. However, the development of modern pesticides has undergone several major milestones over the last four centuries. In the

seventeenth century, sodium sulfate (Glauber's salt) was discovered and became one of the earliest chemical compounds used as a seed treatment against smut diseases of wheat in Europe.

One of the major public health challenges throughout history has been the proliferation of vectors transmitting parasites and pathogens. Among the methods developed to combat these threats, chemical control has become one of the most widely used approaches.

Chemical control consists of the use of synthetic chemical products as repellents, attractants, or insecticides to suppress harmful organisms and reduce contact between hosts and disease vectors. Pesticides—including insecticides, fungicides, herbicides, and related products—have achieved considerable success because of their effectiveness in controlling pest populations.

1. Historical Overview of Insecticide Use

Chemical control has been practiced for thousands of years. Sulfur was already being used in ancient Greece around 1000 BCE, while the Roman scholar Pliny the Elder recommended arsenic as an insecticide.

Around 1200 BCE, the Chinese used insecticidal preparations composed of lime, ash, and plant extracts. Arsenic compounds were later employed extensively for pest control. During the Middle Ages, several poisonous plants, such as aconite, were used against rodents.

In 1690, the insecticidal properties of tobacco were recognized. In India, gardeners used roots of *Derris* and *Lonchocarpus* plants, which contain rotenone, as botanical insecticides. Tobacco extracts were used to control pear psylla as early as the seventeenth century and became widespread in Europe by the beginning of the twentieth century.

Persians were among the first to use pyrethrum, extracted from chrysanthemum flowers, as an insecticide. During the eighteenth and nineteenth centuries, the development of chemical pest control accelerated with agricultural mechanization and the introduction of insecticides derived from pyrethrum and derris.

A major breakthrough occurred in 1874 when the German chemist Othmar Zeidler first synthesized DDT. However, its insecticidal properties were not recognized until 1939 when the Swiss scientist Paul Hermann Müller demonstrated its remarkable effectiveness against

agricultural pests and disease vectors such as mosquitoes. For this discovery, Müller received the 1948 Nobel Prize in Physiology or Medicine.

The first industrial production facility for DDT was established in the United States in 1943. Following World War II, global pesticide production expanded dramatically. By 1951–1952, annual production exceeded 100,000 tons. Continued growth throughout the twentieth century led to worldwide production levels of approximately 1.5 million tons by 1970 and 2.5 million tons by 1985.

Initially, insecticides were regarded as highly effective tools for protecting humans, livestock, and crops from harmful pests. However, concerns soon emerged regarding their persistence in the environment, slow degradation, accumulation in soil and water, and biomagnification through food chains. Many researchers began warning that ecosystems were becoming contaminated by pesticide residues.

During the 1970s and 1980s, a new generation of insecticides—the pyrethroids—emerged and gradually came to dominate the insecticide market. Nevertheless, extensive insecticide use also contributed to the destruction of natural enemies of pests and promoted the development of insecticide resistance.

Throughout the twentieth century, three major groups of insecticides were extensively employed:

A. Organochlorine Insecticides

- DDT
- Lindane
- Chlordane
- Aldrin
- Dieldrin
- Endrin

B. Organophosphate Insecticides

- Widely used in agriculture and public health programs.

C. Carbamate Insecticides

- Developed as alternatives with different modes of action.

From the 1970s onward, pyrethroid insecticides became increasingly important in public health programs. In 1974, the World Health Organization established specifications for insecticides and application equipment, including DDT because of its high effectiveness and low cost. Subsequently, newer compounds with lower toxicity to humans and animals and reduced environmental impacts were introduced.

2. Definition of Pesticides

Pesticides are substances or formulations used to prevent, destroy, repel, or control plant pests, plant diseases, insects, rodents, weeds, and other organisms harmful to plants. They are also used to control insects and external parasites that affect animals and public health.

Chemical pest control generally involves the application of insecticides, acaricides, fungicides, herbicides, and related products, often at concentrations sufficient to suppress harmful organisms and reduce disease transmission.

2.1 Classification of Public Health Insecticides According to Chemical Groups and Their Effects

Insecticides may originate from several sources.

A. Inorganic Insecticides

-Heavy Metals

These compounds are now rarely used because of their toxicity to non-target organisms. They generally act as protoplasmic poisons by precipitating proteins and interfering with enzymatic activity. Examples include copper salts and mercury salts.

-Inorganic Acid Derivatives

These include:

- Fluorides
- Fluorosilicates
- Fluoroaluminates
- Borates
- Arsenites
- Arsenates

Most act as stomach poisons following ingestion.

B. Plant-Derived Insecticides

-Pyrethrins

Pyrethrins are neurotoxic compounds that act primarily through contact.

-Nicotine and Rotenone

-Secondary Plant Metabolites

These compounds may act as:

- Repellents that prevent pest approach.
- Antifeedants that inhibit feeding.
- Direct toxins causing mortality.

C. Classification According to Mode of Action

Insecticides may act through:

-Contact Action

The toxic substance penetrates the cuticle and disrupts physiological functions.

-Respiratory Action

The compound enters through the respiratory system and affects the nervous system.

-Ingestion Action

-Systemic Action

The compound is absorbed by plant roots or leaves and transported through the vascular system.

D. Classification According to Chemical Nature

This classification includes highly diverse and continuously expanding groups, such as:

- Organochlorines
- Organophosphates
- Carbamates
- Dithiocarbamates
- Other synthetic and natural compounds

2.1.1 Organochlorine Insecticides

Organochlorine insecticides are synthetic organic compounds containing one or more chlorine atoms in their molecular structure. Their toxic effects result from several mechanisms:

- Contact toxicity.
- Neurotoxicity.
- Damage to digestive system cells.

These compounds were extensively used between 1940 and 1970 but later declined significantly because of environmental and health concerns.

Organochlorines are primarily contact insecticides and generally do not require transport through plant sap to affect feeding insects. They function mainly as neurotoxins by disrupting sodium channels that are essential for nerve impulse transmission.

For example, DDT affects insects through both contact and ingestion, producing generalized tremors, loss of coordination, and ultimately paralysis. Symptoms may take up to 24 hours to appear.

Although acute toxicity to humans is relatively low under normal conditions of use, organochlorines are characterized by:

- High environmental persistence.
- Strong bioaccumulation potential.
- Formation of stable degradation products.
- Low water solubility.
- Low vapor pressure.

These properties result in long-term accumulation within organisms and ecosystems and lead to biomagnification through food chains. Some compounds persist for many years in soils, plant tissues, and animal fat, which has led to their prohibition in numerous countries.

Their extensive use has also contributed to the development of insecticide resistance, particularly among dipteran insects such as mosquitoes.

Major organochlorine insecticides include:

DDT Group

- DDT
- Perthane
- Methoxychlor
- Dicofol

HCH Group

- Lindane

Chlordane Group

- Chlordane
- Heptachlor
- Aldrin
- Dieldrin
- Endrin
- Chlordecone

- Perchlordecone
- Dinoclor

Terpene Derivatives

- Endosulfan
- Toxaphene
- Polychlorocamphene

Other Organochlorines

- Chlorfenethol
- Mirex
- BHC (Lindane)
- Pentachlorophenol
- Chlorobenside

Among organochlorine insecticides used in public health, **lindane** has historically been one of the most important active ingredients.

2.1.2 Organophosphorus Pesticides

Organophosphorus pesticides are compounds characterized primarily by the presence of a phosphorus atom, usually bonded to one or more sulfur or oxygen atoms. They act as neurotoxins by inhibiting the enzyme cholinesterase, leading to the accumulation of acetylcholine in the insect's body. This causes excessive nerve stimulation and severe muscular contractions, followed by paralysis and eventually death.

The most important active ingredients of organophosphorus pesticides used in public health are **temephos, chlorpyrifos, and malathion**.

The first commercially available organophosphorus pesticide, **parathion**, dates back to 1944. Today, these pesticides represent the most diverse group of insecticides on the market. They share few characteristics except for their origin, a certain degree of lipid solubility, and their mode of action on the nervous system. They are cholinesterase inhibitors that keep the enzyme in an inactive state, resulting in acetylcholine accumulation at nerve synapses, blocking

nerve impulse transmission and causing insect death. This mechanism also explains their high toxicity to humans and warm-blooded animals.

Most organophosphorus pesticides penetrate plant tissues to varying degrees. Some are semi-systemic, while others are transported through the plant vascular system and are therefore systemic. Unlike organochlorines, they are characterized by high acute toxicity but low residual activity. Their low residual effect often requires repeated applications to ensure long-term protection. Due to their high lipid solubility, they easily penetrate the insect body. Some compounds are specifically acaricidal (effective against mites and ticks).

2.1.3 Carbamate Pesticides

Carbamates are synthetic organic compounds derived mainly from **carbamic acid**, which also includes many fungicides and herbicides. Their toxic action is similar to that of organophosphorus pesticides because they also inhibit cholinesterase activity.

One of the main active ingredients among carbamate pesticides is **fenobucarb**. Some carbamates have specific effects, such as insecticidal or molluscicidal activities. **Propoxur, bendiocarb, and dioxacarb** are also used in malaria control.

These compounds generally act by contact, although some have systemic effects, such as **aldicarb** and **benfuracarb**. They generally have low persistence.

The principal classes include:

- **Phenyl methyl carbamates:** aminocarb, BPMC, carbaryl, isocarb, isoprocarb (MIPC), methiocarb, metolcarb (MTMC), mexacarbate, promecarb, propoxur.
- **Heterocyclic methyl and dimethyl carbamates:** bendiocarb, carbofuran, dimetilan, dioxacarb, pirimicarb.
- **Aliphatic methyl carbamates:** aldicarb, methomyl, oxamyl, thiodicarb.

Other examples include benfuracarb, diallate, dimetan, ethiofencarb, fenoxycarb, formetanate, formetanate hydrochloride, mercaptodimethur, and thiofanox.

2.1.4 Pyrethroids

Synthetic pyrethroids, also known as **third-generation insecticides**, are derived from natural pyrethrum plants or from compounds extracted from the flowers of Dalmatian pyrethrum and certain chrysanthemum species, especially *Tanacetum coccineum*, with the aim of increasing their toxicity and photostability.

This family of synthetic insecticides originated from pyrethrins; natural insecticidal compounds found in pyrethrum flowers. These insecticides were introduced in the mid-1970s and are widely used in agriculture, horticulture, households, and public health (including hospitals) to control a broad range of insects. They are also used in skin lotions and shampoos for the treatment of lice and scabies, and in veterinary products against ticks and fleas (ATSDR, 2003).

Pyrethroids can be recognized by names ending in **"-thrin"**, such as **permethrin, cypermethrin, and deltamethrin**.

These insecticides are highly toxic to insects and act by contact, killing them almost instantly through a neurotoxic shock effect, allowing their use at very low doses (10–40 g of active ingredient per hectare). They are highly effective against insects while exhibiting relatively low toxicity to mammals.

Their primary mechanism of action is the disruption of ion channels and synaptic receptors, producing toxic effects on the nervous system. Like organochlorines, pyrethroids kill insects by inhibiting sodium channels necessary for nerve impulse transmission.

They are considered relatively non-toxic to humans and have one of the highest safety ratios (insect toxicity to mammalian toxicity) among chemical insecticides. Acute poisoning symptoms in humans may include respiratory, dermatological, and gastrointestinal manifestations. Since there is no specific antidote, treatment focuses on symptomatic relief.

Pyrethroids are highly biodegradable and do not persist in soil, but they are extremely toxic to certain aquatic organisms, particularly fish, as well as beneficial insects, including bees.

-Potential Sources of Exposure to Pyrethroids and Their Effects

Pyrethroids can enter the human body through:

- Consumption of contaminated food or dust,
- Inhalation after spraying insecticides indoors or outdoors,
- Skin contact, for example when using anti-lice shampoos.

Consumption of contaminated food, particularly fruits and vegetables, is one of the main routes of exposure .

Chronic exposure to pyrethroids may affect fetal and child development, potentially leading to behavioral changes or reduced cognitive performance (Viel et al., 2015). They may also interfere with natural hormones and reduce fertility (ATSDR, 2003).

The **U.S. Environmental Protection Agency (US EPA, 2004)** classified **permethrin and resmethrin** as possible human carcinogens. However, the **International Agency for Research on Cancer** considers the available data insufficient for deltamethrin, permethrin, and fenvalerate, placing them in **Group 3 (not classifiable as to their carcinogenicity to humans)**.

2.2 General Considerations Regarding Long-Term Pesticide Use

- Equipment for vector control operations.
- Indoor residual spraying activities.
- Outdoor insecticide spraying for vector control and public health suitability.
- Guidelines for protecting pesticide workers in tropical climates.

2.3 How to Reduce Exposure to Pesticides During Use

Individuals using pesticides should be aware of potential risks and hazards, possess appropriate spraying and personal protective equipment, and be trained in the proper handling, application, and storage of the chemicals they use.Training should include:

- Proper use of personal protective equipment (PPE),
- Use and maintenance of spraying equipment.

All operators of spraying equipment should wear suitable protective equipment and mix and apply pesticides according to **WHO and manufacturer instructions** to maximize efficiency and minimize risks.

Pesticides should be registered, imported, transported, used, and disposed of according to technical guidelines issued by the **Food and Agriculture Organization (FAO)** in collaboration with the **World Health Organization (WHO)**.

2.4. Indoor Residual Spraying (IRS) – Long-lasting insecticide spraying inside dwellings

Indoor residual spraying limits disease transmission by reducing the survival of mosquitoes inside homes and sleeping areas, as well as on surfaces within buildings where vectors rest, with a high level of spatial and temporal coverage. It involves applying an effective dose of insecticide, usually once or twice a year. The WHO Pesticide Evaluation Scheme currently recommends twelve insecticides belonging to four chemical classes of active ingredients. This is an effective vector control method, especially when implemented correctly. Since residual spraying is not recommended after an outbreak of vector-borne diseases has occurred, spraying must be carried out properly and completely before the start of the disease transmission period, ensuring that all potential vector resting sites are thoroughly sprayed. Indoor residual spraying campaigns should be carried out in the shortest possible time by deploying the maximum number of spray operators. Indoor residual spraying operations should cover at least 80% of houses in target areas.

Mosquito control services have used malathion and fenitrothion for over twenty years as alternatives to DDT, which was considered highly toxic to the environment. In 2006, organophosphates were banned from the list of insecticides permitted for use in public health. This ban was mainly due to their lack of selectivity towards non-target animals and their toxicity to humans. Therefore, pyrethroids are used to treat homes both indoors and outdoors. However, while deltamethrin is among the best insecticides for treating indoor environments, it shows some limitations when used in open spaces. The WHO recommends a dose of 1 g/ha of deltamethrin for spatial treatment of public areas. Studies have shown that this dose of active ingredient, when applied as three treatments with three-day intervals, is no longer effective against pyrethroid-resistant *Aedes aegypti*. Controlling adult mosquitoes through indoor and outdoor spraying requires careful treatment planning, incurs high labor costs, necessitates

continuous vehicle movement, and consumes large quantities of insecticides and other equipment. Clearly, no urban or rural community can carry out such operations without using approved services funded by the state.

2.4.1. Insecticide fumigants

These are used to kill adults, such as dichlorvos, which disperses in the area at normal room temperature. There are also insecticides that kill, irritate, disturb, or repel insects from a distance through airborne effects when vaporized using a heating device. The insecticide can also be released as an aerosol from pressurized spray cans, which are limited in use, i.e., only in poorly ventilated or enclosed spaces.

2.4.2. Long-lasting insecticidal nets (LLINs) – *Moustiquaire à imprégnation durable*

The use of mosquito nets dates back to ancient times, being mentioned in the Bible and in the writings of the ancient Romans. Herod (73–4 BC) mentions that fishermen in Egypt would wrap themselves in fishing nets, as the smell of fish repelled flies and mosquitoes. Chinese accounts dating back to the 3rd century AD attest to the use of mosquito nets by wealthy families in the kingdom. In the 19th century, the era of great scientific and military expeditions, explorers adopted the mosquito net as their preferred weapon against biting insects. Despite their ancient use, mosquito nets only became an integral part of global malaria control programs in the last quarter of the 20th century. The US military used the first DDT-impregnated mosquito nets during World War II. In 1960, the Chinese conducted further experiments on impregnating nets with DDT, but these trials were inconclusive, and research was abandoned. For several decades after World War II, the only weapon against mosquitoes was indoor residual spraying of long-lasting insecticides, a rudimentary tool that proved reasonably effective in protecting people inside their homes. Then, starting in the early 2000s, insecticide-treated nets were added to vector control strategies in many countries.

Long-lasting insecticidal nets are an effective method of personal protection. Insecticide-treated nets with long-lasting effects last longer than conventionally treated nets (twenty washes), which corresponds to about 3 years; nevertheless, they should be replaced regularly. Their use leads to large-scale mosquito mortality. Between 2000 and 2015, one billion nets

were sent to malaria-endemic areas. Permethrin, a pyrethroid, is commonly used and recommended for impregnating nets and clothing, as it has proven highly effective with no known side effects. Nets treated with permethrin or deltamethrin provide humans with unprecedented protection against mosquito bites. Deltamethrin is widely available. Its dosages are much lower than permethrin, but it is more expensive and more toxic to domestic animals and humans; however, the active compound content in formulations is lower, and the type of fabric used in the nets plays a role in reducing harm.

Insecticide-treated nets combine a physical barrier that reduces the density of contact between humans and vectors, and a chemical insecticide that affects vector density and longevity. Thus, these nets add to the individual protection they provide users a collective impact on the vectors' ability to spread, benefiting even unprotected populations due to the high mosquito mortality rate and reduced human-vector contact. Insecticide-treated nets remain the best means of personal protection. An insecticide-treated net provides individual protection when its effect is felt at the individual or household level. When nets are distributed with coverage approaching or exceeding 80%, the insecticidal effect is observed throughout all households. Indeed, the reduction in human-vector contact, coupled with high mosquito mortality, provides community protection, and its benefits are reflected in reduced disease transmission. The use of pyrethroid-treated nets has prompted extensive research in many areas of public health. This research has objectively addressed aspects related to the net itself, the insecticides, and the ethnological and socioeconomic factors that determine the population's acceptance or rejection of this malaria control method. Although pyrethroid-treated nets are currently the best means of protection against malaria vectors, they remain unavailable and too expensive for many in rural areas. Many villages remain isolated to this day, far from transportation routes and urban services. In urban centers, where communications are faster and household incomes are higher, the use of pyrethroid-treated nets may be widespread.

2.4.2.1. Insecticide-treated clothing

Treating clothing with fast-acting pyrethroid insecticides, such as permethrin and cyfluthrin, applied at a rate of 1.25 g per square meter of fabric, irritates or kills insects, which is better than applying them directly to the skin. Their strong adherence to fabric allows for the use of higher doses. Insecticides are preferred over volatile repellents for the following reasons:

- They are fast-acting, repelling or killing insects.

- They have a long duration of action and withstand external factors, sunlight, and washing in cold water.
- Their use is acceptable because they have a mild odor.
- They are safe and do not irritate the skin when used at the correct dosages.
- They are cheaper than repellents.
- They remain effective for weeks or months.
- The active compound does not disappear with sweat, evaporation is slow, and they are not lost through rubbing.

However, treating clothing with fast-acting insecticides remains unavailable and too expensive for many in rural areas. The only real problem facing insecticide-treated nets is the global spread of insecticide resistance. The day will come when even pyrethroids become completely useless. Scientific research is focused on finding new insecticides, combining the best of them to generate synergistic mechanisms, and continuously developing innovative control strategies.

2.4.3. Use of adulticides via space spraying

Controlling adult mosquito stages through aerial insecticide spraying is generally considered a last resort, as these methods pose significant risks to the environment (impact on protected species and food chains); their use must be carefully considered. This involves spraying using ultra-low volume (ULV), fogging, and conventional spray methods. The aim is to kill insects quickly, and its effectiveness lies in keeping insecticide particles (5–50 microns) suspended in the air for a short period. Insecticides such as fenitrothion and malathion, as well as less toxic ones like pyrethroids (including deltamethrin and resmethrin), have been used against adult insects weekly, and fenvalerate, used every two days. They are sprayed in areas where insects are present, such as animal shelters, on animals themselves, and in their resting places, ensuring thorough coverage. Application cycles depend on the vector type, its behavior, the selected insecticide and its concentration, formulation, efficacy, and residual activity duration, the type of sprayed area, environmental and climatic conditions, the disease transmission season, and disease severity. This method requires complex, advanced equipment with precise calibration and adjustment, is expensive, requires trained personnel, and has limited effectiveness because the insecticide remains active for only a short period. Additional measures include:

- Insecticide-impregnated ear tags for animals using pyrethroids.
- Insect repellents such as diethyltoluamide (DEET), commercially available as a repellent.

The use of insecticides in public health relies more on their toxicological and ecotoxicological properties than on their actual efficacy against mosquitoes. It is utterly unreasonable to release toxic substances into natural environments, especially if they accumulate in soil and living organisms. European regulations governing insecticidal products are very strict in this regard. Concerning adulticides, pyrethroids remain the only insecticides authorized for use in Europe. This unbalanced situation does not allow for rational management of control efforts. Consequently, the repeated and widespread use of the same insecticide inevitably generates strong selective pressure, leading to the emergence of resistance mechanisms. Once resistance appears, increasing doses is futile; it only exacerbates resistance and further pollutes the environment.

Developing a new insecticide and bringing it to market requires massive investments from manufacturers. However, the vector control market provides little financial incentive, to the extent that laboratories do not even bother to test its efficacy against mosquitoes when a new molecule is discovered. The emergence of new insecticides effective against mosquito larvae or adults is unlikely in the coming years. In this situation, the only remaining option for managing insecticide resistance is to develop innovative strategies, the most viable of which is combining several compounds with different mechanisms of action.

2.4.4. Insect repellents

A mosquito repellent, or insect repellent, is a product applied to the skin, clothing, or other surfaces to prevent mosquitoes from approaching or landing on the treated area, primarily by affecting their sense of smell. It is not an insecticide: insecticides are substances designed to kill insects, including mosquitoes (63). However, this effect requires contact with the product: substances that only have insecticidal action do not prevent bites.

One of the main prevention methods relies on the use of insect repellents, which consist of active ingredients recommended by national public health authorities, such as DEET, IR3535, picaridin, and *p*-menthane-3,8-diol (PMD). However, despite the effectiveness of certain substances like DEET, users often prefer more natural molecules such as PMD or essential oils. Therefore, it is essential to develop formulation strategies to increase the duration of protection

after application. These innovative formulations include those based on cyclodextrins, micro- and nanoemulsions, liposomes, micro- and nanolipid particles, polymeric micelles, and micro- and nanopolymeric particles.

Skin-applied insect repellents, applied to exposed areas of the body, provide protection lasting from about thirty minutes to several hours. Their effectiveness varies depending on many factors: the nature of the active molecule, its concentration, the product formulation, the amount used, the frequency of application, sweating, concurrent use of sunscreen, or even swimming. Other factors also play a role, such as environmental factors (temperature, humidity, wind), the attractiveness of each individual mosquito, and its sensitivity to repellents. An insect repellent must possess several characteristics, some of which are essential, such as:

- Non-toxic.
- Effective against many mosquito species, especially disease vectors.
- Not absorbed through the skin.
- Does not cause allergies or skin side effects.
- Does not cause side effects when inhaled during application.
- Its effectiveness lasts long enough.
- Chemically stable.

Other characteristics typically demanded by users include:

- Suitable for a wide range of people (adults, children, pregnant women).
- Pleasant odor or odorless, and reasonably priced.
- Leaves no greasy residue on the skin.
- Compatible with sunscreen.
- Resistant to sweat, humidity, and swimming.
- Does not damage clothing (stains, discoloration, wear).
- Does not affect plastic materials (glasses, watches).

2.4.4.1. History of repellent substances

The use of insect repellents likely developed over millions of years. Indeed, among the oldest methods used by our ancestors to repel mosquitoes were the use of smoke or applying mud to the skin. In ancient times, repellents were made by burning sulfur or spreading clay on the body. The Egyptians used mixtures with castor oil (64). Around the same period, the Romans applied a mixture of vinegar, plant secretions, and oil to the body, especially the head and feet, to repel mosquitoes. Burning herbs, such as black cumin (*Nigella sativa*), bay laurel (*Laurus nobilis*), and oregano (*Origanum vulgare*), was used to repel harmful insects .

In 1901, citronella essential oil was discovered, becoming the most widely used insect repellent until the 1940s (66). Its effectiveness has since been demonstrated, particularly against *Aedes aegypti*. It is still used in many formulations. During World War II, the United States spurred research into new repellent compounds to protect its soldiers from vector-borne diseases transmitted by mosquitoes overseas. Thus, in 1944, the US Department of Agriculture discovered DEET (diethyltoluamide) after screening over 7,000 molecules over five years. Initially intended for military use, it was introduced to the public market in 1957. It is considered one of the most effective and broad-spectrum repellents. Subsequently, the search for new repellent compounds led to the synthesis of IR3535 in 1969 by Merck laboratories in Germany. Initially sold in the United States as a skin emollient and moisturizer, it was quickly adopted by fishermen due to its high effectiveness against certain biting mosquito species. It was marketed as an insect repellent in 1975 (66). In 1973, permethrin, a synthetic pyrethroid acting as both a repellent and an insecticide, was marketed. It is a synthetic molecule structurally derived from pyrethrins, natural insecticides extracted from the pyrethrum flower.

During the 1990s, picaridin, or KBR3023, was synthesized by Bayer laboratories in Germany. Finally, Citriodiol®, a registered trademark of the British company Citrefine, was discovered around the same period. This raw material is produced from the essential oil extracted from the leaves of lemon eucalyptus trees (*Corymbia citriodora*), where the citronellal content is converted into the active compound: *p*-menthane-3,8-diol (PMD). Citriodiol® contains at least 64% PMD and is used as an insect repellent (67). These are among the many products currently available on the market. The National Agency for Mosquito Control Services (ANSP) recommends the following active ingredients as mosquito repellents: DEET, IR3535, picaridin (or KBR3023), and lemon eucalyptus oil (*Corymbia citriodora*) hydrate, and its synthetic derivative PMD (*p*-menthane-3,8-diol) (71). To date, all products containing DEET

and most products containing IR3535 have a marketing authorization and a Summary of Product Characteristics (SmPC). Picaridin and lemon eucalyptus oil (PMD) are currently undergoing evaluation at the European level. Products containing these active ingredients have not yet obtained marketing authorization.

2.4.4.2. Main synthetic repellent substances

a) DEET – DEET (*N*,*N*-diethyl-*m*-toluamide) is the standard insect repellent. Indeed, its long history and use by tens of millions of people annually make it the best effective substance evaluated to date. It is a broad-spectrum and highly effective repellent against many mosquito species: *Aedes*, including dengue vectors *Aedes albopictus* and *Aedes aegypti*; *Anopheles*, the malaria vector; as well as *Culex* and *Mansonia* species. It also repels other insects when used, such as sand flies, black flies, ticks (hard and soft ticks), bed bugs, and fleas. DEET is used at concentrations ranging from 20 to 50% depending on the formulation. The duration of protection depends on concentration, but there is a plateau above 50%, with a maximum duration of 8 hours. DEET concentrations used for adults and children over 2 years old range from 30% to 50%, while 10% is used for children between 1 and 2 years old. Since the minimum effective concentration against *Anopheles* mosquitoes is 30%, when the risk of vector-borne disease transmission is very high for children, higher concentrations are recommended for a short period (maximum one month) while adhering to the recommended daily application frequency. For pregnant women, a maximum concentration of 30% is recommended. The mechanism of action of DEET is complex and multifaceted:

a. It acts as an odor mask, i.e., it prevents the evaporation of attractive components present on the skin, such as lactic acid, and prevents mosquitoes from recognizing them.

b. Due to its low vapor pressure, it acts at distances relatively close to its source. When approaching, the mosquito's olfactory system detects it via two different types of receptors, olfactory receptors and ionotropic receptors, as an aversive volatile signal.

c. If a mosquito lands on DEET-treated skin, its gustatory system detects the chemical as an unpleasant bitter signal. DEET has broad-spectrum neurological effects on ion channels and acetylcholinesterase, which may also disrupt insect behavior towards the skin. For this reason, DEET is sometimes also classified as an insecticide.

Although DEET is the best evaluated active substance to date, it remains irritating to the skin and eyes when used at high concentrations or by individuals with sensitive skin. DEET

concentrations of 50% to 75% may cause redness accompanied by bullous skin necrosis and residual scarring. According to toxicity data from the National Institute for Research and Safety, DEET is slowly absorbed through the skin after topical application in humans; due to its lipophilic nature, it can penetrate the skin barrier and reach deeper layers and blood vessels. It has been detected in the blood with prolonged exposure and high concentrations. However, it is completely metabolized and rapidly excreted. DEET shows no genotoxicity in most laboratory tests and does not appear to be carcinogenic in mice and rats. Because DEET is fat-soluble, it readily crosses the placental barrier in pregnant women. However, epidemiological data show no developmental toxicity. Studies have also shown it is not teratogenic in rats or rabbits and does not cause any changes in reproductive parameters in rats.

DEET is an oily compound that may damage synthetic clothing fibers, plastics, and acrylics. Although considered safe, concerns about its potential side effects have led to the development of many DEET-free, more natural mosquito repellents.

b) IR3535 – Known as ethyl 3-[acetyl(butyl)amino]propanoate. IR3535 generally has a lower repellent efficacy than DEET; it is less effective against *Anopheles* mosquitoes compared to *Culex* and *Aedes*. The duration of protection it provides is 10–20% less than that provided by equivalent concentrations of DEET. However, products containing 20% IR3535 provide protection for up to 8 hours. Moreover, it has shown greater efficacy and longer protection time (approximately 10 hours) in some endemic areas, particularly against black flies that transmit onchocerciasis and sand flies that transmit leishmaniasis. This compound is also effective against mites, fleas, and hard ticks. Unlike DEET, it also repels head lice, bees, and wasps.

This molecule is generally used at concentrations ranging from 20 to 35%, depending on the formulation. Unlike DEET, it has a mild or even odorless scent to humans, is non-greasy, and does not damage plastics. IR3535 is miscible with water and cannot be felt on the skin after the product dries. The compound IR3535 activates a specific taste receptor sensitive to bitter compounds and causes aversion in mosquitoes if it contacts the skin. No side effects have been reported associated with this active ingredient, and its toxicological profile classifies it as practically non-toxic. It does not cause skin irritation in rats but causes eye inflammation in rabbits. Despite the proven safety and efficacy of IR3535, there is growing reluctance to use it due to concerns about the adverse health effects of chemical repellents. Many have also reported it is uncomfortable to use and may damage clothing or personal property.

2.4.4.3. Main synthetic repellents of natural origin and natural repellents

Vector control constitutes an essential element in the prevention of infectious vector-borne diseases, which continue to pose a global health threat. Mosquito vector control, primarily based on the use of chemical insecticides, exemplifies the successes, failures, and challenges currently facing scientific research in preparing for the future of vector control. The use of chemicals to control insects and arthropods raises many environmental and health concerns. Therefore, the use of synthetic molecules of natural origin and naturally derived ones with good efficacy represents a suitable alternative.

a) Picaridin – Also known as icaridin or KBR3023, this is a colorless, odorless molecule with low toxicity. It evaporates slowly from the skin, giving it a longer-lasting repellent effect than DEET. However, it is less effective against ticks, some *Anopheles* species, and *Culicoides* midges. The recommended dose ranges from 10 to 20% for short-term protection (3 to 5 hours), and 25% for longer periods (up to 10 hours). Picaridin can be used for children from 24 months of age at a maximum concentration of 25%. It can also be used for pregnant women at a maximum concentration of 20%.

Picaridin is derived from the piperidine molecule, the active component in pepper, from which it derives its name. It is a volatile molecule with an odor unpleasant to mosquitoes, thus forming a protective "cloud" that repels insects, deterring them from contacting the host and thus preventing bites. Like DEET and IR3535, picaridin activates a specific taste receptor sensitive to bitter compounds, causing mosquito aversion upon skin contact. Picaridin may cause eye and skin irritation in individuals with sensitive skin, but it is less toxic and better tolerated than DEET. Studies conducted on animal models in Australia and Europe have shown no skin, organ, or reproductive toxicity. Unlike DEET, this molecule does not emit a chemical odor, leaves no sticky or greasy feel on the skin, and does not damage clothing or plastics.

b) *p*-Menthane-3,8-diol (PMD) – This is a synthetic derivative of lemon eucalyptus oil (*Corymbia citriodora*) hydrate. It is recommended by the National Association of Environmental Service Providers (ANSP) as one of four effective mosquito repellents. The pure manufactured oil is extracted by steam distillation from the leaves of the lemon eucalyptus tree found in South America, China, and Australia. It consists of 74% citronellal, along with other monoterpenes (citronellol, geraniol). However, these compounds are highly volatile, having high vapor pressure. For example, the vapor pressure of citronellal is 0.25 mmHg at 25°C. Therefore, these substances tend to evaporate and dissipate rapidly in the air, resulting in limited repellent activity because very little remains on the skin. Hence, in the manufacture of the

natural repellent product Citriodiol®, citronellal is converted to PMD, which has a low vapor pressure. This increases the product's efficacy in repelling insects. Citriodiol® consists of at least 64% PMD, along with other monoterpenes such as citronellal, citronellol, and isopulegol. The presence of these by-products and residues does not affect PMD's repellent activity but significantly enhances it. Its repellent activity is similar to that of DEET. The CDC and the French Public Health Authority have recommended products containing PMD as an alternative to DEET.

PMD is present in insect repellent products at concentrations ranging from 10 to 40%. One study showed that a formulation containing 20% concentration is effective against *Aedes aegypti* for over 5 hours (82). This product is not recommended for children under 3 years of age, nor at concentrations above 10% for pregnant women. Citriodiol® contains 0.35% terpene derivatives, which may cause convulsive seizures. Therefore, the French National Agency for the Safety of Medicines and Health Products (ANSM) does not recommend its use for children under 3 years of age. However, no poisoning cases have been reported since its introduction, including in children under 3 years of age. The toxicity of PMD has only been partially evaluated. However, it causes severe eye irritation when handled in its pure form.

c) Natural molecules – As natural and environmentally friendly mosquito repellents, there is growing consumer and pet owner demand for options such as essential oils. Essential oils are "preparations" made from plants. They are aromatic products, generally of complex composition, extracted from a botanically defined plant material, either by steam distillation, dry distillation, or by an appropriate mechanical process without heating. The essential oil is often separated from the aqueous phase by a physical process that does not significantly alter its composition. Essential oils have been used for centuries for their various properties, including their repellent properties. Indeed, a wide range of plants have the ability to secrete insect-repellent substances against various arthropods, including mosquitoes, as a defense mechanism to avoid infestation. The efficacy of an essential oil is often not precisely determined, as it is the complex mixture of its components acting in synergy that confers its repellent activity. However, the presence of one or more volatile components (terpenes, aromatic derivatives) is considered essential for its activity. These components include α-pinene, cineole, eugenol, limonene, citronellol, camphor, and thymol. Terpenes are an interesting alternative to mosquito repellents, with the sensory advantage of their pleasant fragrance. A study conducted on 38 essential oils showed that the most effective were citronella oil (*Cymbopogon nardus*), patchouli oil (*Pogostemon cablin*), clove oil (*Syzygium*

aromaticum), and Indian pepper oil (*Zanthoxylum limonella*) (87). These oils provided complete protection for 120 minutes against *Aedes aegypti*, *Culex quinquefasciatus*, and *Anopheles dirus*. Clove oil was more effective than the other three oils, providing protection for 240 minutes against *Culex quinquefasciatus* and 210 minutes against *Anopheles dirus*. Lemon eucalyptus essential oil contains citronellal, one of the most common natural active ingredients in insect repellents, and its chemical structure resembles PMD. The first documented use of this oil dates back to the 1960s, when extensive screenings were conducted on plants used in traditional Chinese medicine. This oil is characterized by a short duration of action due to its rapid evaporation, requiring repeated application. PMD, on the other hand, is a more effective insect repellent and a synthetic derivative made from this oil. Despite its effectiveness when freshly applied, its protective effect fades quickly due to the high volatility of its molecules, providing repellent efficacy for only 20 minutes. The duration of protection can be extended using other natural products in the mixture, such as vanillin. Indeed, many studies show that this compound acts synergistically with essential oils and increases their effectiveness. For example, adding 5% vanillin to catnip essential oil (25%) increased the duration of protection almost threefold, from 45 minutes to 120 minutes. Essential oils should be used with caution. Their use may cause side effects such as skin irritation, allergies, and photosensitivity. Misuse also increases the risk of poisoning. They are strictly prohibited for children under 30 months of age, as well as for pregnant and breastfeeding women. Terpene derivatives, when taken in excessive doses, may cause neurological problems such as seizures in infants. Because they may lower the seizure threshold, they are also not recommended for people with epilepsy.

2.4.4.4. Currently available pharmaceutical forms

Currently, only a few molecules are used in most commercially available insect repellent products. The main difference between these products lies in their pharmaceutical formulation and the research and development efforts to provide a repellent that lasts longer, is better tolerated, and improves the user's sensory experience. Since insect repellents are considered biocides, they must be classified, labeled, and packaged according to this regulatory framework. Therefore, depending on its formulation, a mosquito repellent product may carry warnings and hazard statements, as well as hazard pictograms.

2.4.5. Larvicides

Larvicides are used when access to breeding sites is possible and their number and area are relatively limited. This requires the following:

- Larval control operations using insecticides should be considered as one of the supporting methods for environmental sanitation.
- Targeting vector breeding sites improves the performance of control operations and reduces costs.
- The dose or concentration must be adjusted according to the water source.

The insecticides used include oils such as fuel oil and petroleum oils, which act as a barrier, preventing larval stages from breathing and hindering adults from laying eggs. Other insecticides used include Chlorpyrifos, Fenthion, and Temephos. The use of larvicides to spray running water or during rainfall is strictly prohibited. Insecticides should not be sprayed more than 90 cm from the edge of standing water, nor should they be sprayed in the middle of the water body. To achieve effective results in mosquito control, breeding sites should be treated once every 7–10 days, i.e., 3–4 times per month. Larval control operations are carried out for at least two months during the breeding season. The use of insecticides to treat drinking water wells and reservoirs is prohibited; they should be tightly sealed to prevent mosquito breeding inside them.

Animals are also injected with Ivermectin, known for its ability to kill insects, as it is excreted in their feces and thus also affects larval stages.

Generally, the control of vector and nuisance insects relies on the following recommendations:

1. Focus on measuring insect density before and after insecticide spraying to assess the success of control.
2. Control flying insects using a group of chemical insecticides different from those used for controlling immature stages (pyrethroid compounds with organophosphorus compounds).
3. Control flying insects in public places a maximum of twice a week, according to their density levels, without neglecting waste containers.
4. Control larvae in wet waste collection areas and standing water pools, without overusing residual insecticides to avoid contributing to increased resistance development.

Spraying should be at least every two weeks for residual insecticides and twice weekly for other insecticides.

5. Control flies in the early morning and mosquitoes in the late evening.
6. It is preferable to have two commercial formulations of the same active ingredient to allow for rotation between them.
7. Control crawling insects using insecticide powders, which are dusted and distributed evenly.

2.5. Main insecticides and active ingredients used in Algeria

Algeria relies on various insecticides for mosquito control, mainly focusing on pyrethroids and organophosphorus insecticides with knock-down effects. The most commonly used substances include Deltamethrin, Permethrin, and Malathion for adult mosquitoes, in addition to biological insecticides such as Bti or chemical ones for treating larvae in standing water. Also:

- **K-Othrine** (Polyzone formulation – 6.25% deltamethrin): Widely used in public health for adult mosquito control, characterized by long-lasting residual effect.
- **Pyregrine 5.0 SC**: A liquid pyrethroid insecticide used for surface spraying and thermal fogging indoors and outdoors.
- **Deltacis / Deltacal**: Insecticides based on deltamethrin (25 EC) at different concentrations.
- **Malathion**: An effective organophosphorus insecticide used for the immediate knockdown of adult mosquitoes.
- **Household products**: Sprays and liquids (such as "Sofil" or products based on citronella and pyrethrins) are used for personal protection and mosquito repellency.

Insecticides are selected based on their efficacy against the target mosquito species and the type of application (spraying for adults or water application for larvae) to ensure maximum effectiveness.

2.5.1. WHO-recommended insecticides

- **Cypermac**: Cypermethrin 10% emulsifiable concentrate. A pyrethroid insecticide for public health, non-systemic, acting by contact and ingestion, characterized by long-lasting effectiveness of more than six weeks. Effective against flying and crawling insects harmful to public health, such as mosquitoes, flies, cockroaches, ants, and bed bugs.

- **Defend**: Deltamethrin 1.25% as an ultra-low volume spray. A pyrethroid insecticide for public health, acting by contact and ingestion, used to control insects that have developed resistance to carbamate, organophosphorus, and organochlorine insecticides, eliminating public health pests and household crawling insects such as cockroaches, ants, fleas, bed bugs, and flying insects such as flies and mosquitoes, as well as insects found in warehouses and empty storage rooms. It is also used in animal shelters and has a long-lasting effect.

- **Kovet**: Deltamethrin 2.5% emulsifiable concentrate. A non-systemic insecticide for public health, acting by contact and ingestion, characterized by long-lasting effectiveness. Controls houseflies, ants, bed bugs, cockroaches, mosquitoes, lice, and insects found in garbage collection areas and other flying and crawling insects.

- **Malafos**: Malathion 57% emulsifiable concentrate. An organophosphorus insecticide for public health, acting by contact, ingestion, and inhalation. Eliminates public health pests such as cockroaches, ants, spiders, mosquitoes, crawling insects (silverfish, earwigs, mites), and houseflies.

- **Pergon**: Permethrin 25% emulsifiable concentrate. A highly effective pyrethroid insecticide for eliminating a number of public health pests. A fast-acting insecticide acting by contact. Pergon is formulated to have a long-lasting effect against flying and crawling insects in treated areas, such as cockroaches, ants, flies, and mosquitoes.

- **Permac**: Permethrin 0.5% dustable powder. A public health insecticide acting by contact and ingestion, highly effective against public health pests such as crawling insects (bed bugs, cockroaches, fleas, spiders, silverfish, scorpions), as well as eliminating wasp and ant nests. It is a ready-to-use dustable powder that does not require mixing with water.

- **Temikyr**: Temephos 50% emulsifiable concentrate. An organophosphorus insecticide affecting the insect's nervous system, used to control all mosquito larvae in public health settings, including ponds, swamps, and sewers.

- **Star**: Alphacypermethrin 5% emulsifiable concentrate. An effective pyrethroid insecticide acting by contact and ingestion. An economical and effective insecticide at low concentrations. It can be used for early spraying for prevention, as it has a long-lasting residual effect. It can also be sprayed on walls and insect breeding sites for long-term control lasting up to two weeks. It eliminates many public health pests and household crawling insects such as cockroaches, ants, fleas, bed bugs, and flying insects such as flies and mosquitoes, as well as insects found in warehouses and empty storage rooms. It is also used in animal shelters and has a long-lasting effect.

2.6. Disadvantages and problems resulting from the use of chemical insecticides

Insecticides are designed to eliminate harmful organisms, but some may cause adverse effects on human health. The likelihood of experiencing adverse health effects depends on the type of insecticide and other chemicals it contains, the amount of exposure, and the duration and frequency of exposure. Most often, insecticides affect the nervous system (the system responsible for controlling nerves and muscles). Some adverse health effects of insecticide exposure may appear immediately. Some symptoms may appear several hours after exposure. Other effects may appear after several years, such as cancer. Some symptoms of insecticide exposure disappear once exposure ends, while others may take time to resolve. For people who are regularly exposed to insecticides, long-term health effects are of greater concern. Pregnant or breastfeeding women should consult a physician regarding the possibility of using insecticides in their work, as some may pose a risk to the fetus or infant. The following are the most important disadvantages and problems resulting from the use of chemical insecticides.

2.6.1. Harmful effects of insecticides on humans

- Respiratory irritation, acute throat inflammation.

- Severe coughing.

- Allergic reactions in general.

- Eye irritation.
- Vomiting and diarrhea.
- Headache and occasional loss of consciousness.
- Severe weakness and seizures.
- Liver and kidney diseases and infections.
- Gastrointestinal injuries if the insecticide is swallowed.
- Tuberculosis.
- Certain types of cancer and other serious diseases.
- Birth defects and malformations in fetuses.
- Some genetic disorders and blood disorders.
- Infertility resulting from continuous exposure to insecticides.
- Insecticides cause severe damage to the immune system and the endocrine system and may cause cancer. Fetuses, children, pregnant women, and the elderly are most at risk.
- Insecticides threaten the food chain, and metallic waste from various industrial sources contaminates groundwater.
- Toxic substances cause serious diseases in more than one type of living organism.
- Insects may develop resistance to them over time.

2.6.2. Harmful effects of insecticides on animals

- Animal death as a result of direct exposure to insecticides.
- Bird death from eating plants sprayed with toxic insecticides.
- Animals eating prey contaminated with insecticide residues, causing poisoning.
- Elimination of insects important for the pollination of certain plants.

2.6.3. Harmful effects of insecticides on plants

- Contamination of plants and trees that have been sprayed with insecticides.
- Decline in the presence of some plants due to reduced pollination by certain insects.
- Plants being affected and poisoned as a result of being irrigated with water containing insecticide residues.

2.6.4. Harmful effects of insecticides on water and soil

- Groundwater contamination due to the leaching of toxic substances from insecticides through the soil.
- Direct and severe poisoning and contamination of surface water.
- Soil contamination and stress caused by toxic insecticides.

2.7. Insecticide resistance in vector insects

Insecticide resistance is defined as the ability of some individuals, strains, or species to tolerate a dose of a toxic substance that would have killed the majority of organisms constituting the natural population of the same species, or to survive normally after treatment with a lethal dose of insecticides. This ability results from a selection process for tolerance in individuals within the insect population that have been exposed to the toxic substance over several generations.

Insecticide resistance stems from a genetic—and therefore heritable—physiological, or behavioral adaptation in the mosquito that reduces individual susceptibility to one or more insecticidal products. Mosquitoes have developed four mechanisms of insecticide resistance based on the following adaptations (Figure 13). Figure 13. Main mechanisms associated with insecticide resistance in mosquitoes (based on Anses, 2021).

Resistance arises from genetic modifications leading to mutations that make individuals resistant to insecticides. These new alleles are passed down from generation to generation, and resistance develops within populations through the gradual elimination of susceptible genotypes through successive treatments at the genetic level. Insecticide resistance results from point mutations leading to changes in gene structure and from gene amplification phenomena that alter the production of detoxification enzymes. The development of insecticide resistance is usually attributed to an increased ability of the insect to break down insecticides into less

harmful compounds and excrete them (eliminating them from the body). It may also be related to increased body resistance or changes in composition that prevent the insecticide from reaching its target site, or to the production of larger quantities of insecticide-degrading enzymes. Resistance is a trait based on genetic factors that enable an organism to survive after exposure to insecticide doses that would be lethal to a strain of the organism that has not previously been treated. Resistance genes are naturally present in pest individuals through inheritance and genetic mutations. These genes spread within pest populations through selection processes resulting from repeated insecticide treatments or excessive use. Resistant pest populations emerge from individuals carrying the resistance trait that can withstand insecticide treatments, survive, and reproduce, passing the resistance trait to the next generation, while susceptible individuals are killed. If insecticide treatments continue, the percentage of resistant individuals increases to the point where resistant individuals replace susceptible ones, making the insecticide less effective and, consequently, the control level unacceptable.

Today, only pyrethroid insecticides are permitted for treating mosquito nets, and they are also the most widely used for indoor residual spraying. Although they are less toxic and less persistent than DDT, which was completely banned in 2001, they target nerve cells in mosquitoes, promoting cross-resistance. The systematic use of these insecticides in public health and agriculture has contributed to the emergence and spread of numerous resistance mechanisms among disease vectors, to the extent that the sustainability of gains made in malaria control in Africa is now seriously in question.

Anopheles mosquito resistance to insecticides has been detected in 64 countries worldwide. By 2012, the major malaria vector species had developed resistance to all four classes of insecticides. In 2016, resistance to one or more insecticides was recorded in all WHO regions. For example, malaria vector resistance to pyrethroids is widespread, with 81% of countries reporting resistance.

The use of insecticides remains a cornerstone of current vector control programs implemented against *Aedes* and *Anopheles* mosquitoes worldwide. However, the number of active substances available for public health treatments has steadily declined over the past few decades, and no new molecules will be available in the medium term, reducing opportunities for insecticide resistance management through rotation. In this context, the development of innovative methods for controlling mosquito-borne diseases is an urgent necessity from a public health, environmental, and societal perspective.

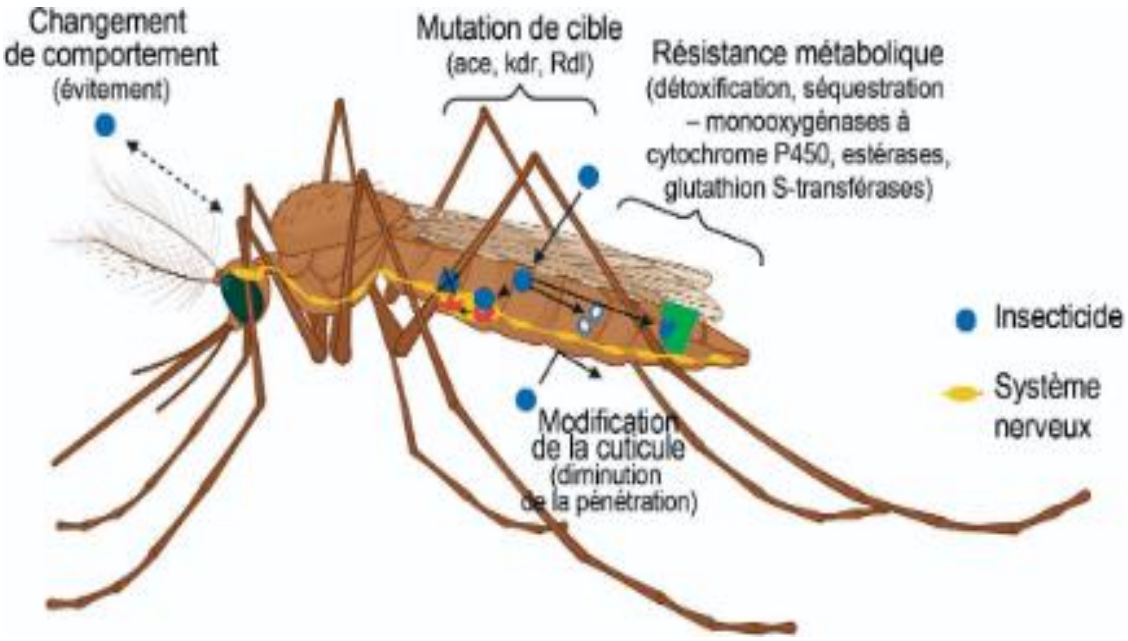


Figure 13. Main mechanisms associated with insecticide resistance in mosquitoes (based on Anses, 2021).

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2.7.1. Some pest control practices that lead to the development of resistance

a. Continuous and repeated use of a single pesticide against populations of a specific pest.
b. Application of usage rates lower or higher than those recommended on the pesticide data sheet.
c. Poor coverage of the treated area.
d. Repeated treatment of organisms with high-density populations and short generation times.
e. Failure to implement non-chemical control practices when conditions allow.
f. Simultaneous treatment of larval and adult stages using a single compound or related compounds.

2.7.2. Causes of the resistance phenomenon

a. Reduced rate of insecticide penetration into the insect's body

The insecticide penetrates the insect's body either through the cuticle or the digestive system. If a change occurs in the pathway or structure of the cuticle or the digestive system (through mutation, for example), this may have a significant impact on insecticide penetration. On the other hand, the external morphological structures of insects may act as a barrier to the entry of toxic substances, such as insects with dense hairs that hinder contact insecticides from reaching the skin and nerve endings. Some scale insects also close their respiratory openings as soon as they detect hydrogen cyanide gas.

b. Rapid excretion of the insecticide from the body

If a lethal concentration of an insecticide penetrates the insect's body, the majority of it can be excreted quickly before it reaches the sensitive system and kills the insect. For example, the American cockroach excretes the insecticide Dimetan from its body without any internal change occurring.

c. Storage of the insecticide in non-sensitive tissues

Some insects can store a quantity of insecticide in tissues that are not sensitive to it. The greater the insect's ability to store the insecticide in non-sensitive tissues, the greater its tolerance. Some studies have shown that some insects store insecticides such as DDT in their fatty tissues.

d. Breakdown of toxic substance molecules and detoxification

After the insecticide enters the insect's body, various reactions occur, some of which convert

the insecticide into a less toxic or non-toxic compound. These reactions occur rapidly before the insecticides can cause tissue damage.

2.7.3. Mechanisms of resistance to insecticide action

Pests use various and diverse resistance mechanisms to survive after exposure to toxic substances. This resistance is often enhanced when pests use two or more mechanisms simultaneously. These mechanisms include:

a. Metabolic (enzymatic) detoxification

This is the most common resistance mechanism in insects, involving the metabolism of toxic substances and their detoxification. It relies on enzymatic systems developed by insects to eliminate natural toxins present in their plant hosts or blood. These systems include esterases, cytochrome P450 oxygenases, and others. Resistant insects may have elevated levels of a specific enzyme or modified forms of the enzyme that metabolize the insecticide at a faster rate than the unmodified enzyme. In either case, the insect can detoxify the insecticide before it kills it. Resistance can range from specific resistance to certain compounds to very general resistance to a wide range of compounds. The level of resistance can range from very low to very high. This mechanism often involves splitting or breaking a molecule of the insecticide or adding molecules such as glutathione transferase, which detoxifies the compound.

b. Reduced target site sensitivity

In this mechanism, the insecticide's binding site is altered so that the insecticide cannot bind effectively, significantly reducing or eliminating its effect. This mechanism is most common in fungi, weeds, and insects.

c. Reduced penetration/absorption

This resistance mechanism slows down the penetration of the insecticide through the cuticle of the resistant insect. This mechanism alone cannot produce high levels of resistance; however, slowing the penetration of the toxic substance can significantly enhance the effects of other resistance mechanisms.

d. Sequestration or compartmentalization of the insecticide

This occurs in plants, where the insecticide is isolated from sensitive parts and stored in other more tolerant sites. It also occurs in insects (such as aphids and *Culex*), where metabolic enzymes are significantly amplified and bind to the insecticide so that it is not metabolized but rather sequestered or compartmentalized.

e. Behavioral resistance

This is limited to insects, acarines, and rodents. It involves a change or modification in the pest's behavior that allows it to avoid the lethal effects of the insecticide. It occurs across all four classes of insecticides, where the insect stops feeding, leaves the treated area, moves to the lower surface, burrows into the plant, or flies away. It is not considered as important as other resistance mechanisms, but it is a contributing factor that helps avoid lethal doses.

2.7.4. Management of insecticide resistance in mosquitoes

A recent Japanese study published in *Science Advances* showed that mosquitoes carrying viruses that cause dengue fever and other serious diseases have become highly resistant to insecticides in some Asian countries, highlighting an urgent need to find new ways to limit their spread. Spraying insecticides in areas where mosquitoes are prevalent is common practice in tropical and subtropical countries. Resistance of mosquitoes to these substances has been a concern, but the scale of the problem has not been precisely determined. Japanese scientist Shinji Kasai and his research team conducted a study on mosquitoes in several Asian countries and Ghana, observing genetic mutations that make some mosquito species immune to widely used insecticides such as permethrin. Kasai noted that in Cambodia, more than 90% of *Aedes aegypti* mosquitoes, the main vector of viruses causing dengue, Zika, chikungunya, and yellow fever, exhibit a range of mutations that make them highly resistant to insecticides. Kasai found that certain mosquito species that were expected to be 100% killed by insecticides now had only a 7% success rate in elimination. Even when sprayed with 10 times the basic amount of insecticide, the mortality rate did not exceed 30%.

Resistance levels vary by region. Kasai noted that the degree of mosquito resistance differs completely between Cambodia and Vietnam.

In another study, Kasai found that insecticides in Ghana and parts of Indonesia and Taiwan remain effective against mosquitoes. The study also showed that the Asian tiger mosquito resists insecticides but to a lesser degree.

a. Resistance reduction strategy

Increasing the dose only increases selection pressure. Similarly, repeating treatments only eliminates susceptible migrating insects that could dilute resistance genes. Therefore, it is essential to focus on operational factors to minimize selection pressure as much as possible. To achieve this, the following is necessary:

- Selecting an insecticide sufficiently different from those previously used.
- Adhering to the recommended application dose.
- Use should be localized in time and space.
- Using products with synergistic effects.
- Diversifying control methods. Many plants have been genetically modified to be resistant to a broad-spectrum herbicide (glyphosate). Consequently, they contribute to the widespread use of this herbicide, exposing plants to the risk of spreading resistance, which has begun to appear in some plants.

b. The need to search for new chemical substances

The study published in the journal *Science Advances* at the end of December 2022, according to expert Professor Cameron, indicated that "commonly used methods will no longer be effective" in controlling harmful mosquito populations. He emphasized the urgent need for new chemical substances and stressed that new ways must be considered to prevent mosquito-borne viruses, such as vaccines. Currently, only a few vaccines are available to combat dengue fever. Indonesia, followed by the European Union, has authorized a vaccine developed by the Japanese pharmaceutical group Takeda, while the use of the vaccine developed by French laboratories Sanofi is very limited because it may worsen disease symptoms in people who have not previously contracted the virus. Dengue infections have increased significantly worldwide over the past 20 years, with between 100 and 400 million cases recorded annually, according to the WHO. Although 80% of cases are mild or asymptomatic, some may face fatal complications.

Kasai, who fears the spread of highly resistant mosquitoes to other countries "in the near future," advised diversifying insecticides as much as possible. However, the problem is that their mechanisms of action on mosquitoes are often similar.

Alternative solutions include intensifying efforts to eliminate mosquito breeding sites or sterilizing male mosquitoes using *Wolbachia* bacteria, an innovative method that has shown positive local results. The location and timing of the emergence of mosquito resistance mutations remain unclear.

III. Biological control

The ease of obtaining and using chemical substances, along with their rapid results, has led to their overuse and misuse. This has resulted in numerous problems, including insect resistance to chemical pesticides, toxic effects on natural enemies, and environmental pollution.

Insecticides are a group of chemical compounds that kill or inhibit the growth of insects, whether synthetically manufactured or extracted from plants, microorganisms, and animals. Today, many types of these compounds are commercially available and have been used effectively and successfully to control numerous insect pests in various parts of the world. However, the widespread use of these insecticides has led to the emergence of many resistant insect strains. Despite the role that pesticides play in pest control, intensive use and failure to follow scientific application methods have led to numerous problems, in addition to the phenomenon of insect resistance to these chemicals.

It is well known that most chemical pesticides are toxic substances, and their harm often outweighs their benefit, especially those with long-lasting residual effects. To reduce the use of these pesticides, many countries suffering from this problem have turned to research to find alternative control methods.

Controlling these vectors remains a crucial element in preventing various vector-borne diseases, especially since they are difficult to control and unpredictable. With growing environmental awareness and knowledge of the dangers of chemical pesticides to human and animal health and environmental safety, biological control has become the only means of preserving ecological balance.

The harmful effects of overusing chemical pesticides on various living organisms and the environment in general have driven researchers to explore safer and more sustainable alternative methods, including biological control.

Biological control is an effective pest management strategy, particularly for crop pests and mosquitoes that pose a public health risk and are responsible for transmitting numerous vector-borne diseases.

Biological control primarily relies on exploiting the natural enemies of pests through the use of microorganisms, plant extracts with biocidal properties, or natural predators such as fish that feed on larvae. These predatory fish are characterized by their ability to feed primarily, or

even exclusively, on aquatic insect larvae, especially mosquitoes. This approach aims to control disease vectors (malaria, dengue, etc.) in a sustainable manner, by targeting their larval or adult stages, or by promoting a balanced ecosystem, or by rendering mosquitoes incapable of transmitting parasites, thus providing an environmentally friendly alternative to traditional insecticides.

Natural enemies are very important factors in maintaining the balance of organisms in terms of their presence and numbers in a given area. Although our country is rich in animal predators living in freshwater environments such as rivers, springs, swamps, and some dam lakes, the use of fish and copepods (crustaceans) in mosquito control has not received much attention. It is also rich in plants whose extracts have proven effective in controlling mosquito larval stages and eliminating them, such as the neem tree (bitter) and others, but research applications are few, if not rare, in this field.

.1. Use of natural enemies such as predators in biological mosquito control

Biological control agents are often an important tool in mosquito control because, when used correctly, they are environmentally friendly and highly effective. They are one of the original biological methods for controlling mosquito larvae and managing larval habitats, thereby reducing disease spread.

.1.1. Insect predators of mosquitoes

There are many species of insect predators of mosquitoes. Service (1967) mentioned aquatic insect predators such as *Microvelia cavicola* and *Paravilia myersi* (Vellidae). Georges and Amin (1987) referred to the use of *Toxorhynchites* mosquitoes belonging to the subfamily Toxorhynchitinae. Nymphs of dragonflies such as *Sympetrum striolum* (suborder Anisoptera), *Coenagrion puella*, and *Ischnura elegans* (suborder Zygoptera) have a high predation capacity for mosquito larvae. The insect *Notonecta undulata* (order Hemiptera) is also an important predator of second-instar mosquito larvae.

.2.1. Larvivorous fish

Freshwater ecosystems are particularly vulnerable to invasive species, and fish are the most widespread aquatic animals in the world.

The biological control of insects of public health concern, such as mosquitoes and black flies, relies on natural enemies such as freshwater fish, which are an effective and environmentally safe biological means of mosquito control by preying on larvae and pupae in standing water. However, the use of fish is not always a legal, practical, or feasible option for mosquito control, as introducing non-native fish species into certain aquatic environments is not only illegal but can also have significant negative impacts on native species and the ecosystem. Many fish species that feed on mosquito larvae, such as minnows, sticklebacks, and golden carp in temperate regions, and in subtropical and tropical regions, most belong to the family Cyprinodontidae. A total of 265 fish species are used to control 35 mosquito species in 40 countries.

The name "mosquito fish" was given to freshwater fish because they feed on mosquito larvae, and they have been used more than any other fish for biological mosquito control. Fish are among the most common predators of mosquito larvae, with species from various genera having been used in biocontrol. However, the two species *Gambusia affinis affinis* and *G. holbrooki* have been used on a wider scale than any other species, having proven their effectiveness in some areas. Furthermore, their breeding does not require complex infrastructure or significant costs, making their use economically viable and easily integrated into integrated mosquito management strategies, provided that their introduction is preceded by a careful environmental assessment to preserve local biodiversity and ecosystem stability.

2-1-1. History of the use of freshwater fish

In the early 20th century, researchers discovered that some fish species naturally feed on mosquito larvae, sparking growing interest in their use for the biological control of these disease-carrying insects. In 1905, American biologist Robert Earle Richardson identified and described the fish species *Gambusia affinis*, which later became one of the most widely used larvivorous fish. Between 1910 and 1930, this species, native to North America, was widely introduced to many tropical and subtropical countries to control *Anopheles* mosquitoes, the vectors of malaria. In the mid-20th century, other larvivorous fish species were discovered and studied in Europe, Africa, and Asia, allowing for greater adaptation of biological control to local environmental conditions. However, between the 1970s and the 2000s, it became apparent that some uncontrolled introductions of larvivorous fish could cause ecological imbalances, such as competition with native species or disruption of aquatic ecosystems. Today, larvivorous fish are still used in some parts of the world as a biological mosquito control tool, but their use

is now subject to a carefully considered approach aimed at respecting local biodiversity and maintaining ecological balance.

.2.2.1. Importance of larvivorous fish

Larvivorous fish play a strategic role in biological mosquito control programs due to their high effectiveness in regulating larval populations, which represent the most sensitive and critical stage in the life cycle of disease-carrying mosquitoes. By feeding primarily on mosquito larvae and pupae, these fish halt the development of immature stages, leading to a significant reduction in adult mosquito populations and thus reducing the risk of vector-borne disease transmission, including malaria, dengue fever, and Zika virus, particularly in tropical and subtropical regions. From an ecological perspective, the use of larvivorous fish represents an environmentally sound alternative to chemical control, as it avoids contamination of aquatic ecosystems with insecticides, limits bioaccumulation and mosquito resistance, and reduces toxic effects on non-target organisms and human health. Furthermore, larvivorous fish species such as *Gambusia affinis* and *Poecilia reticulata* are characterized by their strong predation capacity, high reproductive rate, and great ecological flexibility, allowing them to effectively colonize various aquatic habitats, including stagnant or slow-moving waters such as ponds, pools, rice fields, and irrigation canals. Moreover, their breeding does not require complex infrastructure or significant costs, making their use economically viable and easily integrated into integrated mosquito management strategies, provided that their introduction is preceded by a careful environmental assessment to preserve local biodiversity and ecosystem stability.

.2.2.2. Morphology of larvivorous fish

Larvivorous fish possess a set of morphological, physiological, and behavioral characteristics that explain their high efficiency in preying on immature mosquito larvae. In addition to their small size, typically ranging from 2 to 7 cm, these fish have a fusiform, elongated, and streamlined body covered with fine scales, which reduces water resistance and enhances their rapid and precise movement in shallow aquatic environments. Their superior mouth, often wide and protrusible, is perfectly adapted for capturing mosquito larvae and pupae that gather on or just below the water surface. The pectoral and caudal fins are well developed, providing them with superior maneuverability, rapid acceleration, and high skill in chasing prey. Sensorially, these fish have a highly developed visual system and a lateral line sensitive to vibrations, allowing them to effectively detect larval movements. Coloration varies by

species, sex, and environment, ranging from silvery gray to yellowish green, and may play a role in camouflage or communication among individuals of the same species.

Furthermore, marked sexual dimorphism is often observed, with males being smaller, slimmer, and more brightly colored than females. From a biological perspective, larvivorous fish are also characterized by early sexual maturity, high fecundity, and a rapid reproductive cycle, contributing to rapid population growth. These fish also exhibit high tolerance to environmental changes, particularly in temperature, oxygen, and salinity, which explains their ability to adapt to diverse aquatic environments such as ponds, pools, rice fields, and irrigation canals.

.2.2.3. Main species of larvivorous fish

.2.2.3.1. Gambusia – Larvivorous fish

The emergence of using freshwater fish as predators of the immature stages of mosquitoes (larvae and pupae) living in water has achieved great success in biological mosquito control. The most widely used and introduced freshwater fish for biological mosquito control is the Gambusia fish (*Gambusia affinis*, native to America) (Figures 2 and 3). Interest in using fish for control began after science established the relationship between mosquitoes and malaria and their transmission of many other viral diseases, in addition to other species such as the topminnow and others that are no less important. Furthermore, species such as *Gambusia affinis* are characterized by their strong predation capacity, high reproductive rate, and great ecological flexibility, allowing them to effectively colonize various aquatic habitats, including stagnant or slow-moving waters such as ponds, pools, rice fields, and irrigation canals.

It is a well-known fish widely used to eliminate mosquito larvae, as it is bred to clean ponds of these larvae. It lives in a temperature range of 21–26°C. It feeds on all types of fish food and is also insectivorous. It lives in the Mississippi Basin in Louisiana, USA, and other parts of the world. It is not recommended to breed them in various ponds due to their aggressive tendencies. Females produce 40–80 fry over a two-week period, and parents should be isolated from offspring to prevent them from attacking them. A study on reproductive strategies in *Gambusia heterochir* observed that fecundity is related to increased body size, meaning that reproductive efficiency is directly proportional to increased body size and daily feeding level. The females of these fish use photoperiod to sense the approaching breeding season, requiring at least 12 hours of light to begin entering the reproductive stage at a temperature of 20°C. Males are

continuously fertile after reaching maturity. It was also found that *Gambusia* have a reproductive strategy that has led to the development of many large-sized prey and juvenile fish, resulting in more advantages for *Gambusia*, especially nutritionally, as they feed on zooplankton such as crustaceans, small insects, and mosquito larvae. They are opportunistic predators with a wide dietary diversity, and environmental changes are the main factor that has helped this fish species survive. *G. affinis* can tolerate salinity levels of up to 40 ppt with low toxicity from ammonia and nitrite.

Regardless of the disruption to ecosystems and food chains of insects and animals, the effects of pesticides leach into vegetation. This inspired the Directorate of Fisheries and Fishery Products in the province of Annaba, Algeria, to initiate, in coordination with various relevant directorates, the implementation of a pioneering experiment to cultivate *Gambusia* fish in areas known to be hotspots for mosquito spread and in many wetlands in Algeria, given its geographical location, natural composition, and diverse climate. There are approximately 254 natural wetlands (Figure 7), about sixty of which are of international importance and listed under the Ramsar Convention, within the framework of biological control instead of chemical control. Not far from Algeria, the experience of stocking lakes with *Gambusia* fish has already been carried out by the health authorities and the Casablanca Environment Company at Lake Paradise. These fish belong to the freshwater fish family and have a great capacity to adapt and live in very difficult conditions, such as lack of aeration and high water temperatures. They have become one of the most widespread fish in the world after a large number of countries adopted them as a biological control method against mosquitoes while preserving the environment.

-Use of *Gambusia* in Algeria

It is believed that there are two similar species of *Gambusia* in Algeria: *Gambusia affinis* (western mosquito fish) and *G. holbrooki* (eastern mosquito fish). It may not be possible to distinguish them with the naked eye, but others mention that the second species is the one present. Some academic works mention that both species are present in Algeria, while others mention only *G. holbrooki*. The Directorate of Fisheries and Fishery Products in the province of Annaba aims to initiate, in coordination with various relevant directorates, a pioneering experiment to cultivate *Gambusia* fish in areas known as mosquito hotspots (Al-Washwashah) within the framework of biological control instead of chemical control (2020). The *Gambusia* fish cultivated by several provinces have given very remarkable results in a

number of southern provinces of the country, such as Tindouf and Adrar, among others, through biological mosquito control. *Gambusia* fish are placed in stagnant water and wastewater treatment plants, which are habitats for the spread of certain insects. Currently, in the Ehrer wetland (250 km from Illizi), a cultivation operation of 5,000 units of *Gambusia* fish is underway. A large number of them have been collected from the Jahil oasis in Djanet, in ponds and water bodies, as part of biological mosquito control for the prevention of vector-borne diseases, under the supervision of the Epidemiology and Preventive Medicine Department at Djanet Hospital, in coordination with a specialized pest control institution.

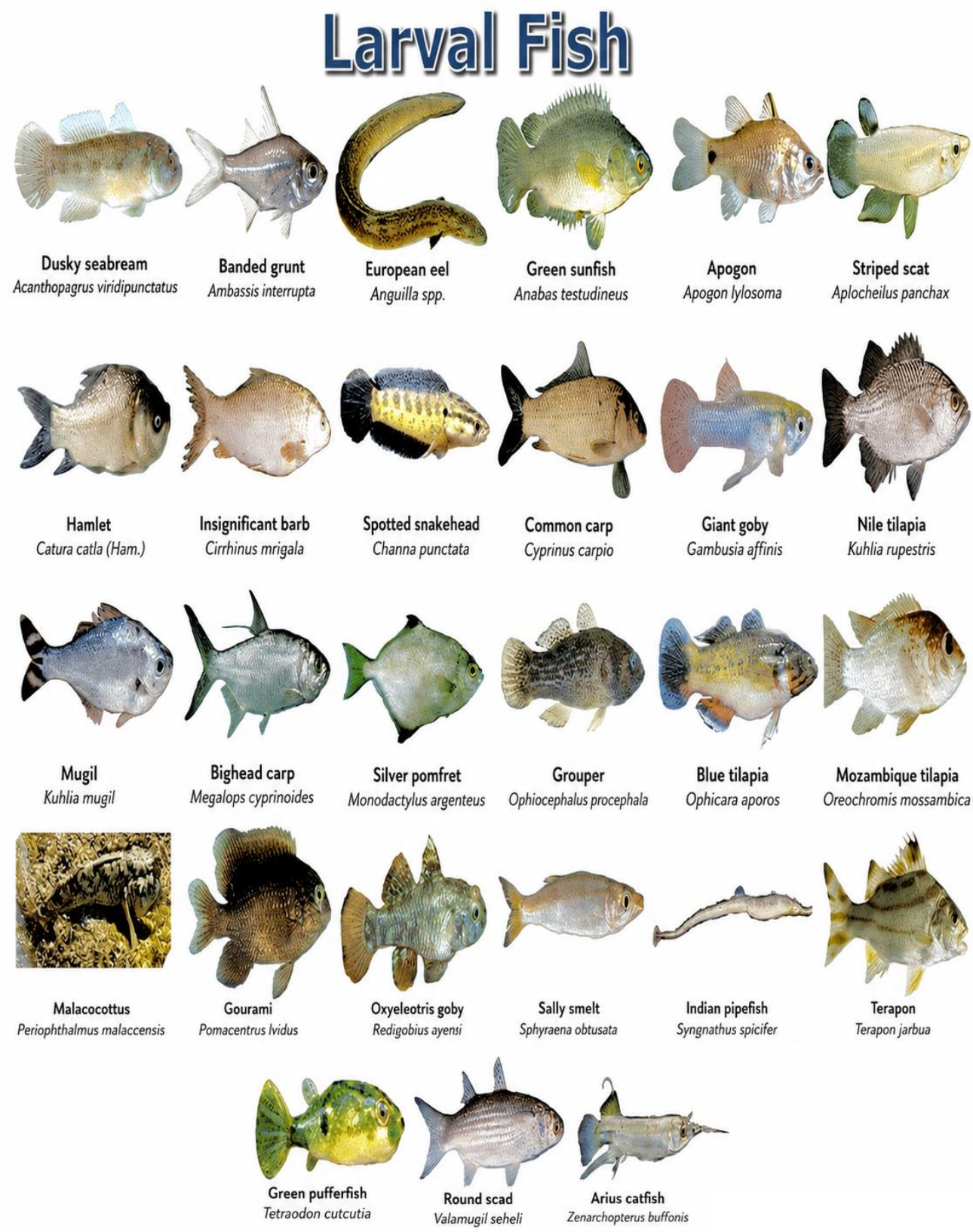


Figure 1 : Main species of larvivorous fish



Figure 3: Male Gambusia fish



Figure 2 : Female Gambusia fish

This operation aims to increase fish populations to combat mosquitoes and harmful insects that are spreading widely in water bodies, especially with rising temperatures. The Gambusia stocking campaign is part of the prevention of insect-borne diseases that breed in ponds and water bodies ranging in length or extent between 300–800 linear meters. This operation is also widespread in southern Algeria, particularly in the El Oued region, which suffers from the spread and breeding of mosquitoes and diseases.

Why has this fish spread and gained such popularity? It is a fast-breeding fish with a great capacity to adapt and live in very harsh conditions, such as lack of oxygen or pollution; thus, it requires no special care or preparation. Regarding its elimination of mosquitoes, it has an upward-facing mouth designed to capture food from the surface (like its relative, the sailfin molly, which is kept in aquariums), where mosquito larvae live. And it is especially... very voracious! This is why it is released not only in private ponds but also in natural water bodies. However, the voracity of this fish is not limited to devouring mosquito larvae; it extends to eating the eggs and larvae of other fish (originally, the mother Gambusia eats her young if they do not hide quickly after birth). Due to its rapid reproduction, ability to tolerate harsh conditions, and this great appetite, Gambusia may threaten the existence of other species because of the aforementioned reasons and due to its competition for available food in the environment. Its aggressive behavior towards other species, including fin-nipping and its consequences, has also been recorded. In Algeria, the threat affects several native (autochthonous) species, and in some cases endemic species, meaning they exist nowhere else

in the world except in our country. Among them are small, beautiful fish of the genus Aphanius, which are found in Algeria—or rather, used to be found—three species: A. fasciatus, A. apodus, and A. saourensis. The last species (A. saourensis), which was found in the Saoura region in Béchar, was declared highly likely extinct during a scientific mission by the IUCN in 2014. One of the main reasons cited for this extinction was Gambusia!

Aquaculturists are in direct contact with the environment, and the term "sustainable development" is not foreign to them. A stocking project must be in harmony with nature and its components, so as not to cause imbalance or any kind of negative impact that may affect native species, which are a treasure that must be preserved and protected from any threat. If stocking involves ponds, pools, or other natural water bodies, attention must be paid and the subject must be studied from this perspective.

Studies showing the negative effects of Gambusia on the local environment of the areas where it has been introduced are numerous. It is classified as a harmful "invasive" fish. This is generally the case for many species that are brought from other regions and released into a new environment for a specific purpose, only to lead to catastrophic consequences that were not anticipated. They reproduce rapidly at the expense of native species and even prey on them. In Algeria, there are several species of this kind, and to our knowledge, their impact on the Algerian environment has not yet been studied, but the negative effects of their stocking have been confirmed in other regions.

Perhaps nature is balanced as it is, and human intervention will only disrupt this balance. Among the native Algerian fish species, there may be good candidates to take on the role of mosquito control without resorting to Gambusia and risking threatening our nature. We therefore call on specialized researchers to pay attention to these species and care for them, as they are not well known and may quietly disappear over time...

For example, the aforementioned Aphanius fish (killifish) have been studied in other parts of the world and have proven effective in eliminating mosquito larvae. Also abundant in the northeastern valleys of the country is the fish Tropidophoxinellus callensis (Maghreb bleak), a social, peaceful fish that reaches about 10 cm in length as an adult, found only in Algeria and Tunisia. From our simple experience in studying their behavior through aquarium breeding, we confirm that they are active and very voracious, and they may perform the required role

perfectly. It remains to be studied academically, which may reveal the possibility of using them as an effective tool in the biological control of the mosquito pest, as an alternative to Gambusia, thereby avoiding potentially serious consequences. And it is not only about fish; our country has endemic amphibians and other organisms, and it would be unfortunate if they disappeared due to our neglect of them.

.2.2.3.2. The Mediterranean killifish or toothcarp – *Aphanius iberus*

The Mediterranean killifish is a species endemic to the Mediterranean coast of Spain. This species may also be found in northwestern Algeria, unless it is a separate species that has not yet been described. The genus Aphanius does not have a worldwide distribution and remains confined to these ecologically specialized areas. In Algeria, this genus is mainly represented by the species Aphanius dispar, a native species. This species inhabits coastal and semi-arid areas in the north and northwest of the country. Its presence is mainly concentrated in coastal areas and the northern plains of Algeria, and sometimes in scattered populations. Both the Mediterranean killifish (toothcarp) and Gambusia holbrooki, biologically and ecologically, live in the Ebro Delta marshes (Spain), have short lifespans, mature early, and spawn multiple times. Killifish are small, generally ranging between 3 and 6 cm in length. Their bodies are short, plump, and slightly compressed laterally, giving them a sturdy appearance. The head is relatively large, with a terminal or slightly superior mouth, adapted for capturing prey on the surface or in open water, especially insect larvae. The eyes are well developed, indicating good visual acuity. Sexual dimorphism is clearly observed in the killifish:

Males often display bright colors with contrasting vertical stripes or blue reflections, especially during the mating season.

Females, on the other hand, are duller in color, tending towards grayish-brown with dark spots that help with camouflage. The fins are relatively short and rounded. The dorsal fin is located on the posterior part of the body.

The killifish is oviparous, with external fertilization. Eggs are laid in large quantities, and this may be repeated several times during the breeding season. The eggs hatch after 7 to 14 days, depending on temperature. The fry become independent shortly after hatching. It lives primarily in coastal and inland aquatic environments, such as ponds, lagoons, salt marshes, estuaries, springs, canals, and slow-flowing streams. It is abundant in both fresh and brackish water, and some species even tolerate high salinity. These organisms are known for their

exceptional ability to adapt to various environmental conditions, such as temperature (from approximately 10 to 40°C), pH (typically ranging between 6 and 9), and low dissolved oxygen levels. This ecological flexibility allows them to survive in unstable and harsh environments. They are used in the biological control of mosquitoes and are considered biological indicators of extreme environments. Many species are threatened due to pollution, habitat destruction, and competition with invasive species such as Gambusia.

The killifish are omnivorous with a tendency towards predation. Their diet includes mosquito larvae and pupae (Culicidae), small aquatic insects, zooplanktonic crustaceans, algae, and organic matter. Thanks to this diet, these fish play an important role in regulating mosquito populations.

Estimates indicate that the killifish has experienced a continuous population decline of at least 50% over the past ten years. Its distribution area, which is less than 500 km², is fragmented and declining due to pollution and the introduction of Gambusia. The two species occupy the same ecological niche, leading to competition. The introduction of Gambusia has caused the disappearance of many killifish populations .



Figure 4 : shows the Mediterranean killifish or toothcarp – *Aphanius iber**us***

2.2.3.4 The guppy – *Poecilia reticulata*

Poecilia reticulata (guppy) is common in tropical regions of South America and the Caribbean. Its natural range primarily includes northern South America, particularly Venezuela, Guyana, Suriname, and northern Brazil, as well as many Caribbean islands. Due to its high adaptability, rapid reproduction, and importance in biological mosquito control and aquariums, this species has been introduced, intentionally or accidentally, to many regions of the world. It is now widespread in Africa, Asia, Southern Europe, Oceania, and Central America. Thus, the fish is now considered a global species, established in many tropical and subtropical aquatic ecosystems around the world.

It is a small freshwater fish with a fusiform, elongated body, laterally compressed, which facilitates its movement in calm waters. Its length generally ranges between 2 and 3 cm in males and between 4 and 6 cm in females. Its coloration varies greatly, especially in males, which display complex patterns (spots, stripes, marbling) and bright colors such as red, blue, green, yellow, and orange. Females, on the other hand, have a silvery gray or brown color, providing effective camouflage. The fins show clear sexual dimorphism:

- The male's caudal fin is often large and well developed, taking various shapes (rounded, fan-shaped, lyre-shaped).
- The dorsal fin is longer and more colorful in males, while it is shorter and less prominent in females.
- The male's anal fin is modified into a tubular reproductive organ specialized for reproduction, while it remains triangular in females.

The guppy is diurnal, social, and very active, living in small groups. It has a high reproductive capacity and a short life cycle, contributing to rapid population growth. This characteristic explains its ecological success, but also its ability to invade certain natural environments. The guppy is a viviparous fish with internal fertilization. The gestation period lasts approximately 21 to 30 days, and each female can give birth to 20 to 60 fry. The fry are independent from birth and reach sexual maturity within two to three months. This characteristic explains its ecological success, but also its ability to invade certain natural environments.

Poecilia reticulata is a freshwater fish found mainly in calm or slow-moving waters such as ponds, pools, ditches, rice fields, irrigation canals, and slow-flowing rivers. It also tolerates brackish water, demonstrating its remarkable ecological adaptability.

This species tolerates a wide range of environmental conditions, including temperatures ranging from 18 to 32°C (optimal around 24–28°C), pH ranging from 6.5 to 8, and sometimes low oxygen levels. It is an omnivorous fish with a tendency towards carnivory. Its diet consists of mosquito larvae and pupae (Culicidae), small aquatic insects, zooplankton (rotifers, cladocera), microscopic algae, and organic detritus. This diet gives it an important role in the biological control of mosquito populations.



Figure 5 : shows the guppy – *Poecilia reticulata*

Successful breeding of the guppy requires providing suitable environmental conditions during the egg-laying period to achieve the highest fecundity rates. The water temperature should be maintained between 20°C and 25°C to achieve the highest growth and reproduction rates, thereby increasing the productive capacity of this fish species. One of the most important recommendations when breeding guppies is that the temperature should not exceed 25°C, as this would become a stress factor for the fish due to the decrease in dissolved oxygen concentration as the temperature rises above this limit. This study concluded that guppies have good tolerance to saline environments, indicating their low sensitivity to salinity.

In Algeria, the guppy is not a native species; it was mainly introduced during the 20th century. The motivation for its introduction was twofold: biological mosquito control, especially of disease-carrying Culicidae, and its use in aquariums. The guppy is now found in

several regions of the country, particularly in northern Algeria, where climatic conditions are favorable.

.5.2.1. Advantages and disadvantages of larvivorous fish

Larvivorous fish are considered a sustainable solution for mosquito control. They provide effective, environmentally friendly, and economical biological control, reducing mosquito breeding and thus the risk of diseases such as malaria, dengue fever, and chikungunya.

- **Advantages:** The use of larvivorous fish offers many advantages for public health and the environment.

First, these fish contribute effectively to the biological control of mosquitoes, limiting the spread of diseases such as malaria, dengue fever, and chikungunya.

Second, this method is natural and non-chemical, reducing the use of insecticides that may be toxic to humans and biodiversity. Furthermore, the introduction of these fish helps reduce public health costs by decreasing the need for medical treatments and chemical vector control campaigns.

Finally, this method is environmentally friendly and sustainable, as the fish can reproduce in their natural environment, ensuring long-term control if suitable conditions are available.

- **Disadvantages:** Despite these advantages, the use of larvivorous fish has some limitations. The introduction of species, especially non-native ones, may negatively affect the local ecosystem, particularly through competition with native species or alteration of the food chain. The effectiveness of these species is highly dependent on environmental conditions: temperature, salinity, oxygen, and the availability of larvae are all factors that affect their ability to regulate mosquito populations. These fish require regular maintenance and monitoring to ensure their survival, reproduction, and continued effectiveness in the ponds and pools where they have been introduced.

Another disadvantage of mosquito fish is that, when food is scarce, they prey on many economically important fish species. The dominance and spread of these fish may limit the growth of other fish species. Additionally, they are susceptible to many diseases and are preyed upon by certain predatory fish. Their effectiveness is also weak in ponds and marshy areas where aquatic plants are abundant. These fish may cause an unpleasant odor in drinking water, and adult fish may eat their young, especially when natural food is scarce.

IV. Microbiological control

Replacing chemical products with biological products is the optimal and most environmentally friendly solution. Researchers and scientists are striving to find effective and available alternatives based on natural products, which are currently experiencing growing interest and increasing popularity. Microbiological control is a form of biological control that uses insect pathogens, such as fungi and bacteria. This aspect of control has been discussed in numerous international studies. Thus, biological control using microorganisms (microbes) is a beneficial sustainable strategy for reducing pests and disease vectors.

Biopesticides are extracted from living organisms (bacteria, viruses, plants, fungi, etc.) or from substances they produce. They are generally harmless in terms of acute toxicity to other organisms in the ecosystem, including humans. Biopesticides are expected to reduce the use of chemical pesticides, and consequently, their use for pest and vector control will increase. There are 250 types of biopesticides worldwide; among them, those based on the bacterium *Bacillus thuringiensis* (B.t) have seen increased use in recent years. 70% of biological plant protection products used are derived from B.t. To maintain their health, humans have always avoided or defended themselves against threats that harm their comfort and economy.

.1. Use of microorganisms in biological control

Infectious diseases in insects arise from the activity of microorganisms within their hosts, associated with the secretion of chemical substances that harm them, or the consumption of the host's food or oxygen in its tissues. The diseased insect shows symptoms such as changes in behavior, body structure, or body color, distinguishing it from healthy individuals. The disease is accompanied by digestive disorders or difficulty in molting to the pupal stage, and the insect rarely emerges from the final instar.

The use of pathogenic organisms in pest control requires precise knowledge of the characteristics of these organisms, their hosts, and the relationship of both to environmental conditions. The host must be present in an environment whose conditions favor the development of the disease, as these conditions increase the likelihood of infection and encourage the presence of insect hosts in high-density populations. There are many organisms pathogenic to insects, the most important of which are:

1. Entomopathogenic Bacteria
2. Entomopathogenic Fungi

3. Entomopathogenic Viruses
4. Entomopathogenic Nematodes

.2. Entomopathogenic Bacteria

Bacteria such as *Bacillus thuringiensis* and *Bacillus popilliae* are among the most important species in microbial pest control, such as *Bacillus thuringiensis* and its various strains: *B. kurstaki*, *B. aizawai*, *B. israelensis*.

In North America, *Bacillus thuringiensis* var. *israelensis* (Bti) and *Bacillus sphaericus* (Bsp) are the main bacteria used as insecticides for mosquito control. They are among the most important strains used in biological pest control.

-1 -2. *Bacillus thuringiensis* bacteria

Bacillus thuringiensis (B.t) is a type of bacterium used for its insecticidal properties. It is a Gram-positive, rod-shaped, facultatively aerobic, spore-forming, and widespread bacterium. It is found in small quantities in almost all soil types, as well as in water, air, and plant leaves. B.t occurs naturally in all soil types. When the spore matures, a toxic crystalline protein forms inside it, becoming a source of infection for insects. When an insect larva ingests the bacterium, its gut wall is damaged, the insect stops feeding, and dies within a few days. After realizing the full potential of B.t bacteria, industry interest in producing biopesticides increased significantly. As a result, in 2010, approximately 90% of biopesticides produced globally consisted of this bacterium. B.t toxin is also used in genetically modified crops (e.g., genetically modified corn and cotton), making it possible to replace chemical pesticides in a wide range of crops, although B.t-resistant pest strains are beginning to become a problem. B.t formulations vary depending on the environment in which they will be used. These formulations are available in various forms, such as granules, capsules, oils, powders, or simply as liquid concentrates.

This species is characterized by its ability to grow on solid or liquid artificial media, and thus it has been possible to produce it in large quantities as wettable powders, emulsions, or dusting powders. The number of different species that can be controlled using preparations of this microbe and its strains reaches about 30 insect species. *Bacillus thuringiensis israelensis* (B.t.i) strains produce a wide range of insecticidal proteins, which are effective against the larvae of many different insects, and in some cases against species from other phyla. This has led to B.t.i-based products becoming the best-selling biological insecticides to date. *israelensis* strains are characterized by being pathogenic to mosquito larvae.

The aforementioned species do not cause disease in humans, farm animals, or plants, and do not harm honeybees or beneficial insects. Bacterial preparations of this species can also be mixed with most insecticides without being affected or losing their properties.

This bacterium produces several toxins and affects, in addition to mosquitoes, black flies and agricultural insects.

The B.t 414 Israeli bacterium is commonly and safely used in drinking water for humans and animals against disease vectors such as *Aedes*, *Anopheles*, and *Culex* mosquitoes, as well as black flies. It is effective, environmentally safe, biodegradable, and has a long shelf life, but its activity period is short, ranging between 24 and 48 hours in the air, thus requiring repeated spraying. Some strains of this bacterium, when mixed with water, dissolve and remain effective for up to 30 days.

.2 .2. *Bacillus sphaericus* bacteria

Bacillus sphaericus is an anti-larval bacterium effective against mosquitoes, producing one type of toxin. It is non-toxic to black flies as well as vertebrates and invertebrates, and is known in most soils and waters. The newly discovered *B. sphaericus* 2362 strain is the most effective. It is also resistant and can be recycled, especially in polluted water. Its effectiveness lasts between 80–90 days in dirty water and 30–50 days in stagnant water. *B.sph* was registered in Canada in 2005 and was first used in a preventive treatment program against West Nile virus. B.sph is a bacterium with effective toxins specifically targeted against *Culex* mosquito larvae. However, the rapid and increasing emergence of resistance to this biopesticide has prompted researchers to deepen their understanding of it in order to improve its use as an insecticide.

.3. History of the use of *Bacillus thuringiensis*

The use of bacteria to control harmful insects does not date back only a few decades, but to 1901.

It is a type of bacterium first isolated in 1901 by Japanese bacteriologist Ishiwata from infected silkworms (*Bombyx mori*). It was described by a researcher in the Thuringia region of Germany in 1911, hence its scientific name, *thuringiensis*.

In France, in 1938, B.t bacteria were first used as an insecticide under the name "Sporein." A B.t-based insecticide did not reach the United States until 20 years later, in 1958.

By the 1950s, *Bacillus thuringiensis* was registered for agricultural use in the United States. In the early 1970s, scientists from the Canadian Forestry Service conducted extensive research to find a way to use it in forests. By the late 1970s and early 1980s, two important discoveries

demonstrated the great insecticidal potential of *Bacillus thuringiensis*. The first was the discovery of the subspecies *israelensis* in the summer of 1976. In Israel, a bacterium with effective larvicidal properties against mosquitoes was discovered in a small pond in the Negev Desert. This bacterium was toxic to mosquitoes and black flies.

Later, the subspecies *tenebrionis*, toxic to beetles, was also discovered. By 1980, Canadian researchers had developed a formulation for applying B.t bacteria that was both effective and economical, as a practical alternative to spraying synthetic chemicals. Sorbitol, a type of corn syrup, was a key ingredient in this formulation and solved many problems. It reduced evaporation during spraying by high-speed, high-altitude aircraft and helped *B.t* bacteria adhere to the needles of sprayed trees. Sorbitol also protected the formulation from contamination and spore fermentation. In the mid-1980s, a new strain of *Bacillus thuringiensis* var. *kurstaki (B.t.k*) was developed and replaced chemical insecticides in aerial spraying to control spruce budworm and other similar insects. Since 1985, it has been the most effective tool against spruce budworm and the most successful commercial product for controlling forest pests globally. Furthermore, the effectiveness of *B.t*. in forest environments and its notable environmental safety have generated significant global interest in the commercial production of this biopesticide for agriculture and other markets.

.4. Advantages of microbial preparations

Bacillus thuringiensis is considered a product of remarkable effectiveness, having practically become the only authorized larvicide in Europe, and its use is increasing globally. The safety profile of *B.t.i*, along with the safety margins associated with recommended operational doses, indicates that its use is safe for micro- and macro-invertebrates, amphibians, fish, birds, and mammals. Finally, *B.t.i* is characterized by low residual activity (a few days) and is therefore considered to have low persistence in the environment.

a- Safe for humans, animals, and beneficial insects.
b- Preserves the natural balance between the pest and its natural enemies.
c- The residual effect lasts for long periods, affecting successive generations (some species).
d- Absence of resistance to microbes (generally, with exceptions).
e- Miscible with chemical and other microbial pesticides.
f- Production of entomopathogenic bacteria is much easier than producing fungal or viral pesticides.

g- Widely used to control insect larvae (Lepidoptera) by producing specialized toxins safe for humans and animals.

.5. Disadvantages of microbial preparations

a- Affected by environmental conditions such as sunlight.
b- Do not provide an immediate effect like chemical pesticides.
c- Require high technical skill from those applying them.
d- Expensive to manufacture (fermentation requires precise expertise) compared to chemical pesticides.
e- The emergence of resistance in some strains recently.
f- The toxicity of pure B.t bacteria to warm-blooded animals is not negligible; inhalation of pure thuringiensin shows significant pulmonary toxicity in laboratory mice.
g- Thuringiensin, or what is known as B.t crystalline toxins, is highly sensitive to solar ultraviolet radiation, leading to rapid degradation. It is also unstable in aqueous solutions, and its half-life decreases with increasing temperature (which reduces its effectiveness).
h- In soil, the toxins produced by the bacteria alter the invertebrate community, and in sediments, they affect benthic organisms, which are a fundamental link in wetland food webs.
i- The use of B.t.i biopesticide for mosquito control has a significant indirect impact on non-target organisms in wetlands, reducing the diversity and abundance of microcrustaceans (e.g., Daphnia), dragonflies, spiders, and indirectly, swallows (by affecting their prey).
j- Finally, the emergence of resistant strains of insects or other invertebrates targeted by B.t biopesticide must be considered in control strategies, especially in the case of large-scale genetically modified crops, particularly when the product is widely dispersed in the environment. Cases of resistance (even high resistance) have been recorded in biting mosquitoes and crop pests.
k- The association of B.sph toxicity with a single type of receptor in the larval midgut explains the ease with which resistance to this toxin can be stimulated, unlike B.t.i, which requires four different receptors.

.6. Uses of *B.t.i* and *B. sph* bacteria in vector control and management

At the beginning of the 20th century, larval control relied mainly on larvicidal oils and pyrethrins, in addition to physical control methods. The discovery of DDT in 1939 and its global

use after the war led to a significant reduction in insect populations and, in some countries, to the elimination of malaria. However, the widespread use of DDT and other organochlorine compounds led to the first cases of insect resistance in the 1950s. Organochlorines were then replaced by other classes of insecticides, such as organophosphates, carbamates, and pyrethroids. The overuse of pesticides, particularly in agriculture and public health, has had serious environmental consequences in the past. The repeated use of chemical pesticides has led to the spread of insect resistance to many types of pesticides, with more than 500 insect species now resistant to at least one pesticide.

Among these species, more than 39% are of medical importance, such as mosquitoes and flies. In the genus *Anopheles* alone, there are more than 50 resistant species, at least 11 of which are important malaria vectors. The development of alternatives to chemical insecticides has become an urgent necessity. The search for specific pathogens has increased in recent years, encouraged by the World Health Organization.

The discovery in 1977 of *Bacillus thuringiensis* serotype B.t.i, which is highly toxic to mosquito and black fly larvae, revived interest in the biological control of vectors. This rise was very rapid for several reasons:

a- The mechanism of action of bacterial toxins (synthesized during sporulation and released into the environment when the bacteria decompose), which attack the larval digestive system, making them effective also against insects resistant to chemical insecticides.
b- The lack of new chemical insecticide molecules to overcome insect resistance.
c- The desire to move away from eradication at all costs, focusing instead on reducing pest populations below an acceptable level by prioritizing environmental control.
d- Increased knowledge over the past thirty years regarding entomopathogenic bacteria, and mastery of B.t production, which was commercially marketed around 1970 to control insect pests in agriculture and forestry.
e- The application method is similar to that of traditional insecticide formulations, allowing for gradual introduction.
f- Ease of producing entomopathogenic bacteria compared to other microorganisms such as fungi or insect viruses.
g- The intrinsic properties of B.t.i, its specificity to mosquito and black fly larvae, its biodegradability, and its notable safety for humans and non-target wildlife.
h- The World Health Organization has been one of the main supporters of the widespread adoption of B.t.i in controlling disease vector larvae, particularly within the Onchocerciasis Control Program (OCP), established in 1974 when black fly larvae became resistant to

temephos treatments. The first B.t.i.-based formulations were applied as early as 1980 in rivers in West Africa.

WHO also encouraged the use of another bacterium, B.s.p, whose toxicity is mainly limited to larvae of the genera *Culex, Mansonia*, and *Anopheles*. This bacterium, which remains highly active in polluted water, is used to treat urban breeding sites and has completely replaced chemical insecticides in some areas. Currently, two main types are commercially available: B.t.i strain 1884 and *B.s.p s*train 2362.

.7. Larvicidal effect of *Bacillus thuringiensis* bacteria

Unlike other subspecies of B.t that require the presence of crystals and spores to cause death in the insect (e.g., B.t *kurstaki* for spruce budworm control, B.t *aizawai* for wax moth control in beehives), the insecticidal effect of B.t *israelensis* comes exclusively from the crystals, which act as a toxin. B.t spores and vegetative cells do not participate in the insecticidal killing process. When the larva ingests the crystals, they partially dissolve in the alkaline fluid of the digestive tract, releasing long protein chains that are different protoxins; hence they are called protoxins or delta-endotoxins (Figure 6, steps 1 and 2). These long protein chains are subsequently cleaved by enzymes (proteases) to produce small molecules of predetermined sizes; these are the toxic fragments, called "toxins." After these toxic fragments are released by the alkaline fluid and intestinal enzymes, these molecules bind to specific receptors present on the membrane of the cells that make up the digestive tract (Figure 6, step 4), anchoring the toxins to the membrane of these cells. Subsequently, due to the biochemical imbalance caused by the toxin activity, the damaged cells swell and burst (Figure 6, steps 5, 6, and 7), causing perforation of the digestive tract wall. The complete loss of digestive tract integrity, resulting from its rupture, appears to be the cause of death in insects poisoned by B.t crystals (the B.t crystal contains at least four toxic fragments, each with its own activity (Figure 6, step 3). Although the mechanism of action of each of these molecules is not fully understood, it is now known that poisoning is the combined result of the action of each of them. Therefore, several steps are required for a toxic effect to occur from B.t crystals. Under natural conditions, i.e., in their environment, the insect, in order to die, must:

- Ingest the B.t crystal, i.e., capture and swallow it.
- Have a highly alkaline digestive tract.
- Possess proteolytic enzymes capable of converting protoxins into toxic molecules.

- Possess suitable membrane receptors, i.e., those compatible with the toxins released by the enzymes.

Most commercial B.t products are based on spore-crystal preparations extracted from a limited number of wild strains.

- *B. thuringiensis* var. *kurstaki* (B.t.k) – which produces Cry1Ac, effective in controlling many insects that feed on tree leaves, which are crop enemies or forest pests that cause defoliation.
- *B. thuringiensis* var. *aizawai* – which produces slightly different Cry toxins and is particularly effective against lepidopteran larvae that feed on stored grains.
- *B. thuringiensis* var. *sandiego* and *B. thuringiensis* var. *tenebrionis* – which produce Cry3Aa toxin and are used to control beetles harmful to agriculture.

B. thuringiensis israelensis – which contains Cry4A, Cry4B, Cry11A, and Cyt1Aa, used to control mosquitoes that can be vectors of diseases such as dengue fever and malaria.

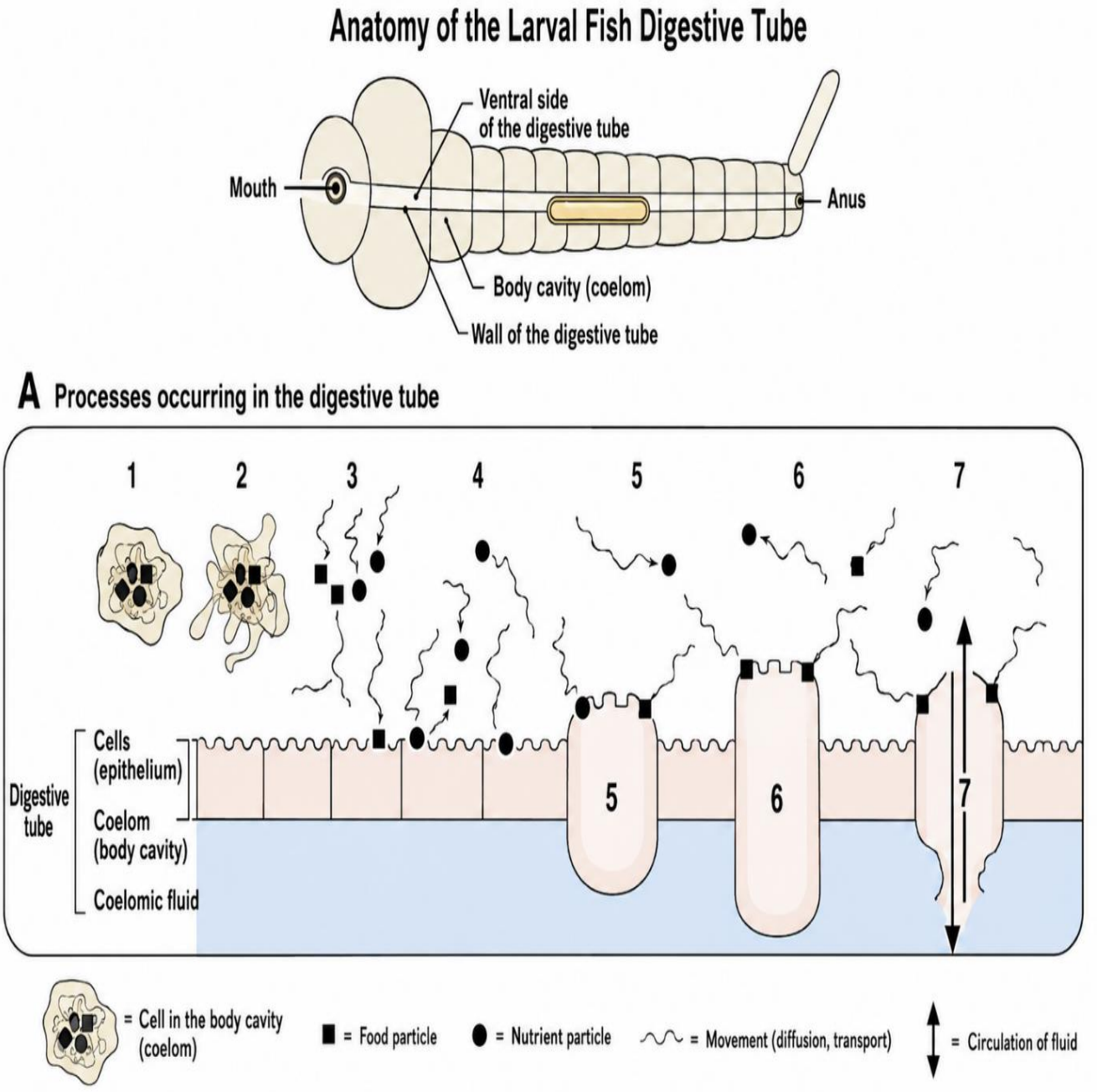


Figure 6: Mechanism of action of B.t crystals on mosquito larvae.

8. Commercial formulations of *Bacillus thuringiensis* bacteria

B.t bacteria are cultivated by fermentation in a scientifically developed medium. The composition of the culture medium and all environmental factors are adjusted to ensure optimal production, promoting the greatest number of germination, reproduction, and spore formation cycles.

Generally, formulations can be classified into solid products (dustable powders, wettable powders, granules, etc.) and liquid products (oil-based, emulsifiable concentrates, aqueous solutions, suspension concentrates, etc.). The choice of formulation depends on the target insect, the type of environment to be treated, ease of access, and the required duration of toxic effect.

.8.1. Solid products

The biopesticide has critical properties, including particle size, bulk density, and flowability. Powdered products are manufactured using carriers such as clay minerals, starch polymers, dry fertilizers, and ground plant residues. Their manufacture and marketing have led to the emergence of various types of granules. These formulations provide high protection for B.t products from ultraviolet radiation and rain. They are commonly used in agricultural crops (cabbage, corn, etc.). Their particle size is generally very fine, ranging between 50 and 100 micrometers, which improves their adhesion to surfaces. However, these granules pose a risk of inhalation toxicity to the user. Another type of solid formulation has also been developed (compressed tablets). These are blocks ranging in size between 100 and 250 micrometers. Their formulations use organic polymers such as polyvinyl alcohol to provide buoyancy, leading to extended toxin release over several months. These tablets have solved the problem of the persistence of B.t-based products in aquatic environments.

.8.2. Liquid products

Other liquid formulations have been developed. These are suspension concentrates based on B.t bacteria. Their composition consists of 10 to 40% microorganisms, 1 to 5% dispersing agent, 3 to 8% wetting agent (short-chain surfactant), and 35 to 65% carrier liquid (oil or water). Depending on the type of carrier liquid, surfactants are characterized by a hydrophilic-lipophilic balance. The advantage of using this type of concentrated formulation is the reduction of transport and storage costs. The development of encapsulation technologies for B.t-based products represents a significant technical advancement in the field of biopesticides. These formulations are mostly liquid, but are also available in powder and granule forms.

This technology provides protection against harsh environmental conditions (UV radiation, rain), resulting in slow release of the manufactured products. Thus, encapsulated products overcome the problem of their stability, reducing application costs.

.9. Safety of *Bacillus thuringiensis* bacteria

Since the beginning of the use of B.t bacteria (over 40 years ago), a large body of scientific studies has established a strong scientific consensus regarding their safety (unknown, 2021). As mentioned earlier, this bacterium is considered a product of remarkable effectiveness, having practically become the only authorized larvicide in Europe, with its use increasing globally.

The safety profile of B.t bacteria, along with the safety margins associated with recommended operational doses, indicates that its use is safe for micro- and macro-organisms, amphibians, fish, birds, and mammals. Long-term studies in Minnesota, Sweden, France, and Germany have shown no direct or indirect effect of B.t bacteria on secondary consumers. B.t.i is specialized in certain species of Diptera belonging to the suborder Nematocera, including mosquitoes and black flies, and is completely harmless to mammals. Analytical studies of 77 studies examining the effect of *B.t.i* on 616 non-target species showed that 15% of species were affected by *B.t.i* treatments, but most responded to doses 5 to 1000 times higher than those used. Finally, *B.t.i* exhibits low residual activity (a few days) and is therefore considered non-persistent in the environment. However, B.t.i spores, the resistant bacterial form, can be found for several weeks to several months after treatment. Because this bacterium is considered non-competitive compared to other soil bacteria, recycling of *B.t.i* has been considered unlikely.

.9.1. Humans and mammals lack the necessary structures to activate the toxin present in *B.t.i* bacteria, so it is safe for them.

In its 2006 re-evaluation of *B.t.i* registration, the Pest Management Regulatory Agency (PMRA) stated: Consumption of treated products is not expected to pose a risk to the general population, children, or infants. The risk of exposure through drinking water is very low. The low toxicity and proven safety of *B.t.i* indicate that human exposure through drinking water does not pose a significant risk. Furthermore, no adverse toxic effects, infection, or pathogenicity were observed through oral, inhalation, intraperitoneal injection, or dermal routes. There appears to be no known toxin or metabolite of *B.t.i* that is an endocrine disruptor or has immunotoxic effects. It is important to note here that the RRFA has access to the full list of ingredients (including those protected by trade secrets) for each registered formulation. Human health and environmental toxicity studies are conducted on these formulations, and thus their results include the effects of additives or adjuvants. The US Environmental Protection Agency (EPA) also concluded that it is reasonable to believe that dietary exposure to B.t residues is safe for infants and children. The WHO Pesticide Evaluation Scheme (WHOPES) published a report in 2009 authorizing its direct use in drinking water to control certain

mosquito species in countries where diseases such as malaria and yellow fever are endemic. This clearly demonstrates that the product is completely safe for humans.

.9.2. For the environment

B.t.i bacteria only become toxic when they reach the stomach of mosquito or black fly larvae. Therefore, B.t.i has no effect on other insects such as honeybees, nor on fish, birds, or mammals. The US Environmental Protection Agency considers the risks posed by B.t.i strains to non-target organisms to be negligible or non-existent. The insecticidal toxin also biodegrades rapidly in the environment through sunlight and microorganisms.

.9.3. Criteria and factors affecting the effectiveness of *B.t.i* bacteria on mosquitoes

.9.3.1. Species

Different mosquito species show varying levels of susceptibility to B.t.i crystals. Generally, *Culex* mosquito larvae are the most susceptible, while *Aedes* larvae are equally or slightly less susceptible. *Anopheles* larvae are the most resistant when exposed to the same amount of B.t.i crystals. This difference in susceptibility also exists within the same genus and is thought to result from behavioral and physiological differences (Aly et al., 1988), but is clearly related to the behavior of the crystals in the environment (Mulla, 1990). Generally, *Aedes* and *Culex* larvae feed actively throughout the water column of the pond, and since *B.t.i* crystals settle slowly, larvae of these two genera are able to ingest a lethal amount. On the other hand, *Anopheles* larvae, which feed primarily on the pond surface, may not have enough time to ingest a lethal amount of crystals, as these crystals settle to the bottom. However, this relative susceptibility can be modified using an appropriate formulation. If *B.t.i* crystals are used in a floating formulation, *Anopheles* larvae show higher mortality rates (Ali et al., 1987). Although there are differences in the type and number of receptors among different mosquito species. According to Mahmoud (1998), *Anopheles* larvae ingest ten times less food per unit time compared to *Aedes* larvae. Therefore, feeding behavior is one of the main reasons for differences in susceptibility. This partially explains the difference in susceptibility between these two species *to B.t.i.*

.9.3.2. Larval stages

Generally, younger larvae are more susceptible than older larvae. As larvae age, their susceptibility to the same amount of B.t.i crystals decreases significantly. Second-instar larvae are 1.5 to 5 times more susceptible than fourth-instar larvae, which feed very little because they have begun to pupate. Pupae are not affected at all by B.t.i crystals because they do not feed, and thus larvicide treatment cannot kill all individuals.

.9.3.3. Temperature

In cold water, the same amount of B.t.i crystals generally results in lower mortality rates. This decrease in toxicity is due to reduced activity. Metabolic changes are observed when the insect is exposed to minimum temperatures close to those of its environment.

.9.3.4. Light intensity

The effectiveness of B.t.i crystals in killing larvae decreases when exposed to intense light, a factor that affects larval behavior.

.9.3.5. Larval density

Achieving the same mortality rate (e.g., 90% of larvae) requires a larger amount of B.t.i crystals when the number of larvae per unit volume is high. Typically, to achieve the same mortality rate, a pond with high larval density (50–100 larvae/liter) must be treated with 1.5 to 2 times the amount of product required for a pond with low larval density (5–20 larvae/liter). In practice, doses are determined based on the surface area to be treated, not on larval density.

.9.3.6. Presence of particles and organic and inorganic pollution

Generally, the more organic matter and suspended colloidal materials present in the habitat, the more *B.t.i* crystals are needed to maintain the same mortality rate. The availability of *B.t.i* crystals decreases when their adsorption onto particles is followed by slow settling. Reduced ingestion rates have been observed in larvae exposed to high concentrations of nutrient particles; they appear to feel full (and ingest fewer crystals, reducing their mortality rate). The presence of high concentrations of chlorine and iron appears to reduce the toxic activity of B.t.i crystals. Organic pollution has a similar effect.

.9.3.7. Water depth

Generally, the deeper the pond, the more B.t.i larvicide crystals are needed to achieve the same mortality rate, as larvae of many mosquitos species feed near the surface. The

effectiveness of different formulations is affected by the availability of B.t.i crystals in the first 10 cm of the water column. In a pond, significant water flow reduces the availability of B.t.i crystals by diluting the product and displacing the insecticidal mass from the treated area.

.9.3.8. Vegetation cover

The presence of vegetation around and over the pond can intercept sprayed liquid, powder, or granule insecticide formulations during application, reducing the availability of B.t.i crystals. In practice, formulations with varying granule sizes are available to deal with different types of vegetation cover.

.10. Environmental effects resulting from *B.t.i* treatment

.10.1. Effects of *B.t.i* on non-target animals (biological and infectious risks

The environmental safety of insecticides must be primarily assessed by monitoring the immediate response of isolated individuals or groups of organisms, as well as by studying potential effects on non-target animals (communities living in the same habitat as the target species). These effects mainly include phenomena of persistence and accumulation within the habitat, as well as disruptions to the food chain. Indeed, living communities are characterized by countless trophic links between the species that compose them.

Generally, the more diverse this network, the greater the ecosystem's ability to manage the temporary loss of one of its links... During the approval period for *B.t.i*-based products in the 1980s, many government bodies around the world (Canada, the United States, Europe, etc.) recognized their short- and long-term safety (for humans and any other mammals that might be exposed). Although there are some studies suggesting a potential effect of *B.t.i* use, no scientific evidence has yet been established of any adverse environmental effects. On the contrary, a large and diverse body of scientific studies, including long-term studies, has demonstrated the safety of *B.t.i*, even in the context of routine use. It is also important to consider the situation in Quebec, where more than 80% of mosquito control operations are carried out only once in the spring. In the French Camargue region and the Rhine Valley in Germany, more than ten major control operations are carried out throughout the year.

- **.10.1.1. Effects of *B.t.i* larvicide on chironomid flies**

In addition to adjuvants, whose adverse effects on non-target animals have been demonstrated, a study conducted on amphibians in Argentina found that B.t.i larvicide suffers from the disadvantage of persisting in the environment and being toxic to other species of Diptera, such as chironomid flies, which are closely related to mosquitoes. Among the few affected species that share the same habitat as the target species. Several studies have shown an effect on chironomid populations. However, these studies were conducted in the context of overdosing. At the doses specified on the labels of products used to control biting insects, B.t.i larvicide shows no effect on chironomid populations. Furthermore, a six-year study in a floodplain of the Dalälven River in Sweden showed that B.t.i had no significant effect on the abundance and diversity of chironomids. Other studies have also shown that although chironomids are sensitive to B.t.i, their numbers are not necessarily affected by treatments.

10.1.2. Effects of B.t.i larvicide on amphibians

A 2015 study reported a potential effect on amphibians in cases of overdosing. Since then, two other studies published in Germany in 2018 and 2019 have refuted the results of this study, as no mortality or growth effects were recorded (et al., 2018). Several previous studies had already indicated no direct or indirect effects of *B.t.i* larvicide on amphibians.

.10.1.3. Effects of B.t.i larvicide on birds

A large body of research confirms that mosquitoes are not a significant prey item for insectivorous birds or bats. Studies analyzing stomach contents show that the diet of predatory birds (insectivorous birds and bats) consists of only 1% mosquitoes, regardless of the high mosquito density available. The energy gained is too minimal to allow predators to feed on these small insects (unknown, 2022). Only one recent study conducted in the Camargue region showed a negative effect of *B.t.i* treatments on the egg masses of the house martin (*Delichon urbicum*). However, this study is controversial, and the observed effect is attributed to the insecticide treatment itself, particularly due to the noise from aircraft during spraying, rather than specifically to *B.t.i* bacteria.

.10.1.4. Effects of *B.t.i* larvicide on mammals

Experimental exposure of mammals to B.t bacteria via oral, respiratory, subcutaneous, or ocular routes has not resulted in any adverse effects. Some commercial formulations containing

B.t.i caused conjunctival irritation in rabbits, but, according to the authors, this appears to be related to the abrasive nature of the product rather than the microbial agent itself. Cases of skin irritation have also been observed. Furthermore, injecting animals with the bacteria usually causes few problems, except in cases of high-dose exposure. In 1998, the US Environmental Protection Agency, based on a review of all published studies, stated that no adverse effects on mammalian health had been observed. These studies were conducted via various exposure routes, including oral, pulmonary, dermal, ocular, and intraperitoneal injection.

Another independent study used *B.t.i* bacteria via the same exposure routes mentioned above, in addition to intracerebral injection and inhalation. It concluded that intraperitoneal injection is the only route that may be lethal to mice at very high doses (10^7 bacteria per mouse), a result insufficient to consider the bacterium a mammalian pathogen. In 1998, the US Environmental Protection Agency, based on a review of all published studies, stated that no adverse effects on mammalian health had been observed. These results are unlikely to be extrapolated to humans, as the experimental concentrations used far exceed what an exposed person could inhale – 100 million times (based on the number of spores/kg of body weight) in the case of a forest worker. It should also be noted that experimental exposure has shown that delta-endotoxin is non-toxic to mammals unless the basic conditions of the insect digestive system are simulated experimentally at high doses. In the late 1950s, some volunteers ingested relatively large doses of *B.t.i* bacteria without showing any adverse effects. The absence of clinical symptoms can be specifically explained by the fact that delta-endotoxin is not activated by the acidic pH of the mammalian stomach.

.10.2. Effects of *B.t.i* larvicide on humans

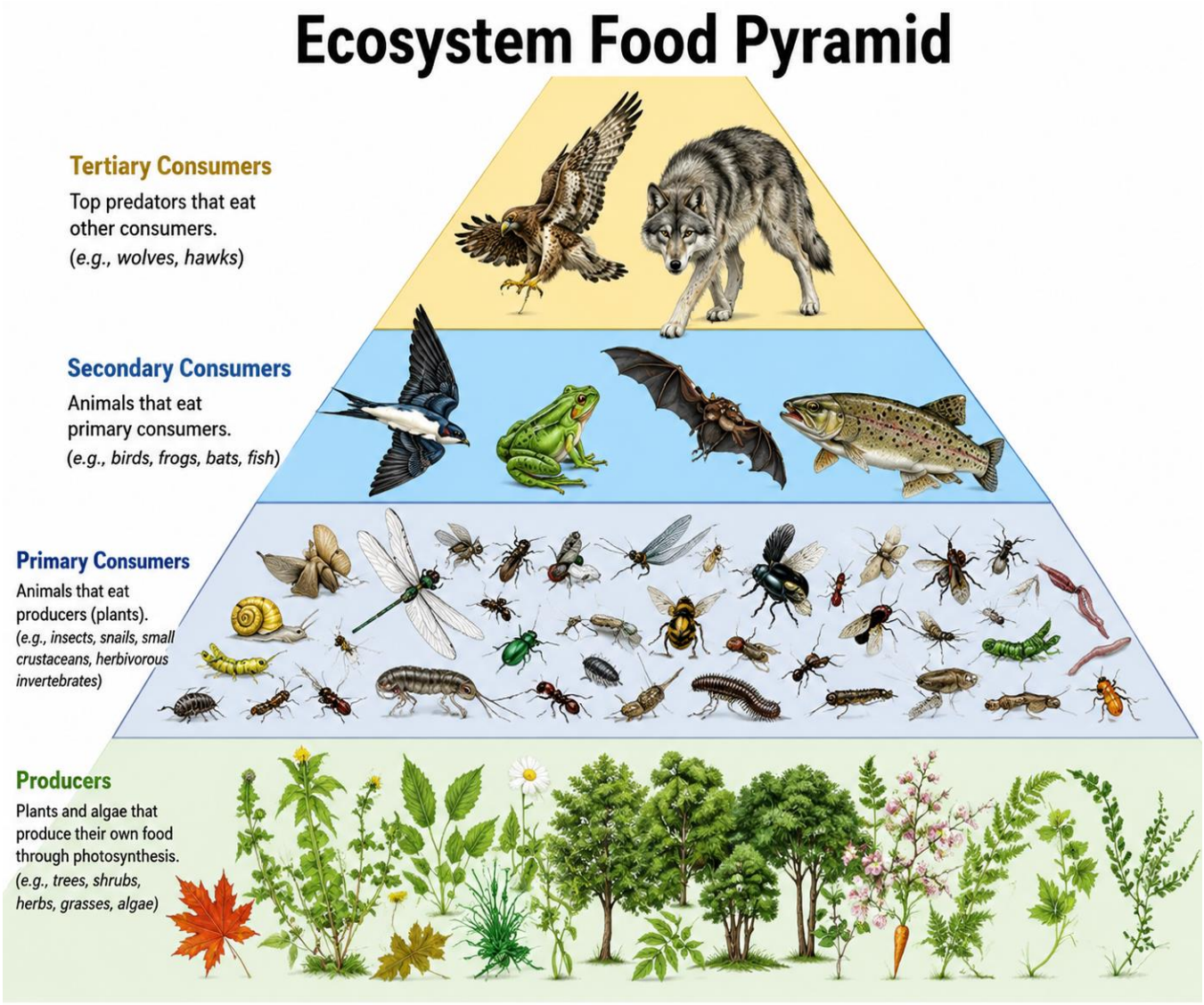
One case of corneal ulcer and one case of lymphangitis were recorded after accidental inoculation with *Bacillus thuringiensis*. A US study conducted on several groups of agricultural workers exposed to different levels of B.t bacteria showed that 50% of the most exposed group experienced a local allergic reaction after skin testing (atopic hypersensitivity), compared to 15% in the other groups. Tests conducted on approximately ten commercial biopesticide formulations containing B.t bacteria showed the ability of all strains to produce a diarrheal toxin (necrotic enterotoxin) of the same type as that produced by *Bacillus cereus*, responsible for food poisoning, although at lower concentrations. However, the inability of *B.t* spores to germinate in the human digestive tract suggests that their ingestion does not pose a significant risk to human health, although no specific risk assessment has been conducted.

Furthermore, the possibility that immunocompromised individuals (particularly those with AIDS, undergoing cancer treatment or organ transplants, burn victims, newborns, and elderly people in declining health) are more susceptible to B.t infection has been considered. These patients are more susceptible to infections from microorganisms generally considered non-pathogenic to humans. However, many researchers believe that immunocompromised individuals may be a preferred target for opportunistic infections caused by *B.t* bacteria.

.10.3. Effects on the food web

Several studies have measured the effect of *B.t.i* bacteria on the entire food web (invertebrates, mosquito predators, nesting birds) in the short and long term. Although a decrease in the abundance of some species is periodically observed, this does not appear to have a lasting effect on the ecosystem. In wetlands, a balanced ecosystem includes a food web in which black fly and mosquito larvae do not constitute the sole food source for aquatic predators. The more diverse the food web, the less likely the complete or partial elimination of a single species will have serious consequences.

In the case of biting insect control, the reduction in biomass is only partial and temporary, as treatments are only carried out when larvae reach a certain stage of development, making them available to predators for a long period. Moreover, larvae remain available in the environment for some time during treatment, serving as a food source for stoneflies, other aquatic insects, and fish. The interval between treatments also allows biting insects the opportunity to recolonize the environment and reappear a few days after treatment. The impact of biting insect control on the food web is limited, given its effect on a highly diverse ecosystem with large biomass (Figure 7).



10.4. Effects of treatment on aquatic ecosystems

The effects of insecticide treatments, whether single or repeated, on non-target animals are usually assessed in natural or semi-natural environments. By sampling the water column and natural and artificial substrates, changes in animal behavior, composition, and biomass can be monitored before, during, and after insecticide treatment. This not only allows for the detection of chronic effects of *B.t.i*, but also potential effects on the structure of the ecosystem's food web and the relationships between different food sources and consumers. Short-term studies analyze effects observable for a few days or weeks after treatment. Increased drift density is the most obvious effect of any type of larvicide treatment on black fly populations.

Toxic effects usually appear within less than two hours. After *B.t.i* treatment, an increase in the number of live, dying, or dead black fly larvae in the drift is observed, along with an increase in the numbers of some non-target invertebrates, particularly certain species of mayflies, caddisflies, mosquitoes, stoneflies, and butterflies. Researchers add that it is difficult to assert that changes in the drift of organisms other than black flies are directly related to *B.t.i,* as they hypothesized that the inert components in the formulation may play a role in causing this drift. Some of these changes may be attributed to differences resulting from the sampling process, rather than an effect attributable to *B.t.i.* Studies examining the short-term effects of *B.t.i* treatments on black flies in temperate regions have shown no statistically significant difference in drift or benthic populations attributable to the effect of this bacterium... except for the study by Hershey et al. (1998), which suggested a possible decrease in the number of predator species. The vast majority of studies concluded that no adverse effects were observed on the growth and structure of non-target communities during mosquito control treatments. In addition to the financial aspect, the main problem associated with medium- and long-term studies, which require repeated monitoring over several months or even years, lies in the ability to distinguish between potential effects of repeated treatment and natural changes in the observed populations and communities.

Establishing research projects aimed at the systematic study of the long-term effects of insecticide treatments is extremely complex under purely experimental conditions. As for drinking water*, B.t.i* treatment, as mentioned earlier, *B.t.i* bacteria were designed for use in aquatic environments. Therefore, they are not assumed to accumulate or spread in soil. The spores of these bacteria do not travel with water to other locations in the soil. For example, during floods, spores do not appear to be transported from treated areas to untreated areas. These effects of B.t.i bacteria on water are consistent with the results of previous studies. It is important to note that B.t.i is harmless to humans, as humans lack the necessary structures to activate the toxin it contains. Furthermore, although B.t.i bacteria cannot be applied directly to drinking water due to strict pesticide laws, the WHO Pesticide Evaluation Scheme published a report in 2009 authorizing its direct application to drinking water, demonstrating that the product is completely safe for human consumption. Moreover, a 2011 study conducted in a Swiss wetland wildlife reserve showed that after 22 years of treatment, it is completely safe for the environment and does not contaminate untreated areas.

.10.5. Persistence of *B.t.i* bacteria in the environment

When discussing the persistence of B.t.i bacteria in the environment, three elements must be considered: the persistence of the toxic effect of the crystals, the persistence of the crystals as a protein mass, and the persistence of the bacteria in spore form. Numerous studies indicate that B.t.i persists in soil mainly as spores, and shows very little multiplication of vegetative cells. B.t.i crystals and spores are present in the aquatic ecosystem for a period exceeding their toxic activity period. The exact lifespan of the bacterial crystal is not known, but it is similar to that of other organic materials such as hair, bones, and insect skins. The bacterial crystals eventually decompose, and their components (amino acids) are recycled within the ecosystem. Furthermore, solar radiation, especially ultraviolet rays, causes rapid degradation of the spores produced by the bacteria. Repeated use of the bacteria also does not lead to their accumulation in the soil.

.11. Development of resistance to *B.t.i* bacteria

Biopesticides based on B.t.i bacteria are characterized by a complex mechanism of action that Is not fully understood, and includes, in particular, the activation of toxins after ingestion, followed by their binding to specific receptors in the digestive tract of insect larvae. The toxins produced by the bacteria differ in their mechanisms of action, particularly Cry4A, Cry4B, Cry11, and Cyt1A, which are known for their synergistic effects. Resistance to bacterial toxins is rare in the natural environment, and its mechanisms are not always known. Regarding B.t.i bacteria, the only field report indicating specific resistance in a vector concerns resistance observed in a natural population of *Culex pipiens* in New York. However, no other study has confirmed this resistance or identified its mechanisms.

The absence of resistance in mosquitoes and black flies, despite the widespread use of B.t.i for many decades, is often explained by the fact that the many toxins act as a mixture, or even synergistically, where selection for populations resistant to multiple toxins is less likely than selection for populations resistant to a single toxin. This multiplicity of toxins and their synergistic effect may also lead to the emergence of more complex, and possibly multifactorial, resistance phenomena. Resistance to individual B.t.i toxins has been achieved in laboratories within a few generations in *Culex quinquefasciatus* and *Aedes aegypti*. This confirms the advantage of using a mixture of toxins with different mechanisms of action. However, it is possible that resistance mechanisms to each B.t.i toxin may appear sequentially and subtly without a noticeable effect on the overall resistance to B.t.i. In areas where this biopesticide is widely used in Germany, a mosquito control program using B.t.i has been in place since 1981.

Over these years, it is estimated that 189 generations of *Aedes vexans* have been exposed to selective pressure from *B.t.i.* A recent study showed no emergence of resistance in sites treated for 36 years. These results are consistent with those of Da Silva Carvalho et al. (2018), who found no resistance after exposing 30 generations of *Aedes aegypti* to *B.t.i.* While resistance to individual toxins can develop in laboratory populations of a given species, no resistance has been observed in wild mosquito populations after decades of treatment with the *B.t.i* biopesticide (Da Silva Carvalho et al., 2018).

We conclude from this that there is no detected resistance in nature against B.t.i. The complexity of the pathogen's mechanism of action with the target insect means that the likelihood of resistance developing in the insect is low.

Conclusion

We have just observed that mosquitoes are among the insects that easily adapt to various conditions. Humans have long believed they could control their blood-sucking enemy by spraying insecticides, which undoubtedly had a clear effect on the transmission of endemic diseases, but also had adverse effects on all treated ecosystems. However, these insecticides allow, in most cases, effective control of mosquito and black fly populations. At present, it is no longer possible to ignore that the choice of insecticide, its selectivity, its mechanism of action, and its application are crucial to the success or failure of a control campaign.

Natural phenomena regulating vector populations play an important role in preventing disease transmission. Furthermore, biological control has proven its effectiveness through the use of *Bacillus thuringiensis* var. *israelensis* bacteria. This type of biopesticide will be used more widely in the future, provided that effective methods are adopted for selecting various additives to overcome the obstacles, particularly environmental and economic ones, that hinder the expansion of biopesticide use. Current trends are towards maximum effectiveness with minimum dosage. Generally, there are two types of formulations: solid and liquid, each with its uses and target markets. These products can serve vector control programs more effectively by replacing all insecticides to which vectors have developed resistance. The costs of using these new insecticides must also be considered, as they often determine the feasibility of control campaigns in developing countries. At a time when humanity is becoming increasingly aware of the need to protect its environment, these insecticides must be as selective as possible. Therefore, these products are subject to numerous and increasing specifications, and new insecticides rarely combine this many properties. Finally, in conclusion of this work, we quote a sentence not written by an entomologist or a doctor, but by astronomer Carl Sagan in 1981:

"Nature has willed that we should enjoy understanding, and those who understand more increase their chances of survival." This is a crucial idea, considering that millions of men, women, and children still die every year from diseases and famines, partly due to insects.

V. Physiological control using insect growth regulators

The side effects of neurotoxic insecticides (contamination of various environments, huge quantities of insecticides used, emergence of resistant species, impact on beneficial insects and pollinators, contamination of food chains, etc.) and environmental imperatives (preservation of human and animal health) have driven the search for alternative methods for pest and disease vector control (improved chemical control, biological control, integrated pest management). Chemical control remains the primary means of controlling insect pests and disease vectors.

The aquatic environment includes the ecosystems most affected, directly or indirectly, by toxic elements. These elements cause, on one hand, deterioration of water quality, and on the other hand, contamination of living organisms through bioaccumulation in the food chain, threatening public health and the environment.

The resistance of vector insects to many conventional chemical insecticides has led the World Health Organization to coordinate an extensive research program to promote the discovery and evaluation of new insecticidal compounds suitable for use in public health. Among the new compounds selected are growth regulators with a mechanism of action completely different from that of conventional insecticides.

A growth regulator is an active substance, natural or synthetic (such as plant hormones), that affects plant growth. It is used to modify growth by stimulating or inhibiting certain physiological processes (cell elongation, flowering, ripening), without being toxic to the plant. The term "growth regulator" can also refer to insect growth regulators (IGRs), which are compounds used in public health or in homes to prevent the growth and reproduction of harmful insects (a chemical substance that affects insect growth). These products offer many advantages over traditional insecticides, particularly high specificity and low toxicity to beneficial insects and mammals. They affect physiological and biochemical processes specific to target organisms, such as chitin synthesis (benzoylurea derivatives) or, through interaction with receptors (dibenzoylhydrazine derivatives), ecdysone synthesis (imidazole derivatives). They also disrupt insect growth, development, and reproduction by interfering with their hormonal regulation.

.1. General information about growth regulator analogs

Growth regulators are classified among modern alternative insecticides, on which great hopes are placed. The control strategy using growth regulators, also known as insect growth

regulators (IGRs), is based on understanding the mechanism of action of hormones that regulate the growth of all living organisms. Hormones, even in minute doses, have a significant effect, and it is known that introducing external hormones into the body can cause disturbances in hormonal balance, leading to significant physiological disorders. Therefore, it can be considered that introducing hormone mimics into the environment may produce similar effects.

Insect growth regulators (IGRs) used in the pest control industry include juvenile hormone analogs and chitin synthesis inhibitors. IGRs do not affect the nervous system; rather, they are insecticides that disrupt vital physiological functions related to insect growth, development, and reproduction (egg production). IGRs are generally not toxic to adult insects, as exposed adults usually suffer no adverse effects and live a normal life cycle. Because they target unique biochemical pathways found only in insects and related arthropods, products containing IGRs are generally characterized by low toxicity to mammals (i.e., $\alpha < 0.05$ values).

.2. Mechanism of action of insect growth regulators

Insect growth regulators are specific substances designed to break the life cycle of harmful insects by interfering with their hormonal system (molting and chitin synthesis hormones). In the context of disease vector control (mosquitoes, ticks, fleas, cockroaches), they prevent larvae from developing into reproductively capable adults or prevent them from emerging from eggs.

During their growth, insects molt several times. They form a new exoskeleton (or membrane) beneath their old one, then shed the old one to allow the new one to reach its final size and harden. IGRs prevent insects from reaching maturity by interfering with this molting process. This slows the spread of pests because immature insects cannot reproduce. IGRs kill insects more slowly than conventional insecticides because they prevent insects from molting rather than directly killing adults. Death usually occurs within three to ten days, depending on the type of IGR, the insect's growth stage at the time of product application, and the insect's growth rate. Some IGRs prevent insects from feeding for a long period before death.

An insect growth regulator (IGR) is a substance that disrupts the growth of harmful insects by mimicking their hormones. These substances specifically target larvae and eggs, preventing their molting or metamorphosis, while being very safe for mammals. These insecticides do not kill insects immediately but can stop the reproduction of harmful insect populations until they are completely eliminated. They are generally used as insecticides to control populations of harmful insects such as cockroaches, fleas, and mosquitoes. IGRs are specific to target insects and are characterized by low toxicity to non-target species. Based on their mechanism of action,

commercially available IGRs are classified into three categories: juvenile hormone (JH) mimics, ecdysone agonists, and chitin synthesis inhibitors. Hormonal IGRs generally work by mimicking or inhibiting juvenile hormone, one of the two main hormones involved in insect molting. These regulators can also inhibit the second hormone, ecdysone, whose high concentrations stimulate insect molting. When juvenile hormone is active at the time of molting, the insect molts into a larger larval stage; in its absence, it molts into a pupa or an adult incapable of growth. IGRs that mimic juvenile hormone can cause premature molting of immature stages, disrupting larval development. They can also affect eggs, causing sterility, behavioral disorders, or disrupting diapause, the process by which insects enter a resting state before winter. Endocrine growth regulators that inhibit juvenile hormone production can cause premature molting of insects into non-functional adults, and those that inhibit ecdysone can cause pupal death by disrupting the normal transformation of larval tissues into adult tissues during the pupal stage.

Juvenile hormone is an insect-specific hormone that regulates growth, reproduction, diapause, and many other aspects of insect physiology. Juvenile hormone agonists (JHAs) and antagonists (JHANs) cause serious disruption of the endocrine system, leading to abnormal larval growth and deformities, and subsequently death.

2.1.Juvenile hormone analogs or regulators

These molecules mimic the insect's natural juvenile hormone. By artificially maintaining a high hormone level, these molecules prevent the insect from reaching adulthood, thus hindering its reproduction and metamorphosis. Examples: *Hydroprène*, *Méthoprène* (*Pyriproxyfène*).

2.2. Examples of growth regulators

. 2.2.1.Methoprene and pyriproxyfen

are two active substances belonging to the class of insect growth regulators (IGRs). They act by mimicking insect juvenile hormone, thereby blocking metamorphosis and preventing larvae from developing into fertile adults.

. Comparison of the two molecules

Methoprene (often used in its S-methoprene form)

Inhibits larval development (particularly in fleas and mosquitoes) and possesses ovicidal activity.

• Common uses: Widely used in veterinary medicine against fleas (often combined with fipronil in spot-on enile hormone analogue, treatments) and in mosquito control . • Profile: Well-tolerated by mammals, but potentially toxic to certain aquatic organisms (crustaceans).

It is a widely used product: in 2012, in the United States, it was present in approximately 500 different insecticides either as a primary active ingredient or as a supplement to other pesticides to enhance their activity or limit the risk of resistance developing. Due to its solubility in both water and fat, as well as a certain degree of persistence, it appears capable of causing ecotoxicological problems—particularly in water, wetlands, and even the sea, where pesticides dispersed in the environment eventually end up via soil runoff. This product acts like a hormone, meaning it is effective at very low doses; consequently, there is a high risk of water contamination in the event of an accident during the preparation of spray mixtures or their application, or due to improper equipment cleaning methods or poor management of "residual mixtures."

2.2.2. Pyriproxyfen

Preventing insect larvae from molting into adults and sterilizing the females, it is indicated for the treatment and prevention of flea infestations. A next-generation juvenile hormone analogue; more active at lower concentrations than methoprene. It also sterilizes adult females (which transfer the product to their eggs or oothecae). • Stability: Highly photostable, providing excellent residual activity both indoors and outdoors. • Common uses: Pest control against fleas and cockroaches in the home, veterinary treatments, agricultural crop protection (whiteflies, scale insects), and public health (mosquitoes). • Precautions: Requires greater environmental caution, as its margin of toxicity for certain non-target organisms is narrower than that of methoprene.

2.3. Chitin synthesis inhibitors

- These substances prevent the production of chitin, a major and essential component of the insect exoskeleton (cuticle). This prevents the insect from molting properly, leading to its death. Examples: *Noviflumuron*, *Hexaflumuron*, *Diflubenzuron*.

- **A. Ecdysone disruptors (ecdysone agonists)**

- These molecules mimic the molting hormone (ecdysone) or cause an early hormonal surge. This forces the insect to molt before it is ready, hindering its growth and leading to its death.

- The action of chitin synthase inhibitors can occur through several mechanisms. Some inhibitors bind directly to the chitin synthase enzyme, blocking its active site and preventing it from catalyzing the polymerization reaction. Others may interfere with the enzyme's regulatory mechanisms, affecting its activity and stability. Yet another approach involves the use of molecules that mimic the substrate of chitin synthase, acting as competitive inhibitors that prevent the actual substrate from binding to the enzyme. Each of these mechanisms ultimately disrupts the production of chitin, leading to weakened cell walls in fungi or compromised exoskeletons in insects, resulting in their death or reduced viability.

  Chitin synthase inhibitors have a wide range of applications, particularly in agriculture and medicine. In agriculture, these inhibitors are used as fungicides and insecticides to control the growth of pathogenic fungi and crop-damaging insects. Fungal infections in crops can lead to significant yield losses and economic damage, and chitin synthase inhibitors offer a targeted approach to managing these infections. By disrupting the cell walls of fungi, these inhibitors can effectively control fungal growth and reduce the spread of infections.

Other studies have indicated that many essential oils and their components are characterized by properties similar to juvenile hormone and act as insect growth regulators. These essential oils have been reported to cause growth disruption and affect insect reproduction. Based on these properties, plant essential oils can be considered natural sources of JHA and JHAN compounds.

To evaluate the effect of essential oils as insect growth regulators, various methods have been used and described in numerous studies. These studies evaluated changes in growth and reproduction (Chaubey, 2008), disruption of biosynthesis (Athanassiou et al., 2014), oviposition deterrence (Elhag, 2010), insect weight (Anshul et al., 2014), hormonal disruption (Maggi and Mangeaud, 2005), insect fertility (Maggi and Mangeaud, 2005), biochemical biomarkers (Sammour et al., 2011), protein and lipid levels (Senthil and Sehoon, 2006), and insect deformities.

However, the use of selective products, biopesticides, and insect growth regulators (e.g., Diflubenzuron, an insecticide used in Algeria for forest pest control) is increasing.

In conclusion, the tested chitin synthesis inhibitors are effective against many pests and vectors or nuisance agents. The unique and specific mechanism of action, selectivity, and low environmental toxicity risk of these new-generation insecticides make their use compatible with integrated pest management and insecticide resistance management programs. However, like all insecticides, IGRs must be handled safely and applied with great care and consideration for non-target organisms. For example, the growth physiology of many invertebrates...

- ## B. Example of Chitin synthesis inhibitors

2.3.1.Diflubenzuron

A benzoylurea insecticide (Benzoylurea (IRAC group 15). commonly used to control leaf-feeding caterpillars and forest pests (sold as *Dimilin*). Contact and stomach poison that disrupts cuticle formation during molting. Pest control in agriculture, forestry (such as the pine processionary moth), and public health (mosquitoes, flies). In public health, used to treat mosquito larval breeding sites (Culex, Aedes, Anopheles).

-Safety and Effects

Human toxicity: Considered unlikely to be carcinogenic, but prolonged exposure may -induce hematological effects (such as methemoglobinemia).

Environment

Low toxicity to mammals and fish, but active against aquatic and beneficial arthropods (observe application rates and areas). For detailed local toxicological analyses,

2.3.2.Triflumuron

is an insecticide belonging to the benzoylphenylurea family, used as an insect growth regulator (IGR) and, more specifically, as a larvicide against mosquitoes.

-Chitin inhibitor: It blocks chitin biosynthesis, preventing normal cuticle formation during larval molting.

-Delayed action

It does not kill larvae instantly; the lethal effect is generally observed 3 to 5 days after treatment (when the larva attempts to molt).

-WHO recommendation

The World Health Organization (WHO) recommends its use against mosquito larvae at dosages ranging from 0.1 to 0.5 mg/L.

C. Advantages and specific features

Ecological targeting: It generally spares adults and offers a more environmentally friendly alternative to conventional neurotoxic insecticides.

-Duration of action

It has a notable residual effect (often lasting several weeks, depending on the formulation, such as 48% SC).

-Limitation

It acts exclusively on immature stages (larvae) and is ineffective against adult mosquitoes.

VI. Control using plant extracts

Since the beginning of creation, plants have been one of the primary sources for meeting human needs. Just as humans obtained food from plants, they also used them for many therapeutic and cosmetic purposes. Since ancient times, humans have used aromatic plants and their extracts in religious rituals, perfumery, cosmetics, industry, and food preservation. They also used them in the preparation of medicinal drugs, which form the primary basis for what science has achieved today in the pharmaceutical industry.

The first evidence of the manufacture and use of essential oils dates back approximately 3000 years before the birth of the Minaean era.

In 1928, a scientist discovered in one of the Pharaonic tombs earthenware vessels containing essential oils dating back 3557 years.

Subsequently, essential oils spread to other civilizations, including the Greeks, Romans, and Byzantines. The Byzantine civilization allowed the establishment of the foundations of distillation. In the Arab civilization, essential oil became one of the main products for international marketing. About 1000 years ago, the Persian physician and scientist Avicenna precisely descrid the steam distillation process, and both Iran and Syria became the main centers for the production of various types of aromatic extracts.

In 1928, René-Maurice Gattefossé coined the term "aromatherapy," and in 1937 he dedicated a book to aromatherapy.

.1. Essential oils

Essential oils are secondary metabolic products extracted from aromatic plants and found in various parts of the plant (flowers, leaves, stems, roots, fruits, peels, etc.). This type of oil is characterized by its easy separation from the plant organs that contain them through various distillation and extraction methods. They are given several names:

- **Essential oils** due to their aromatic fragrance.
- **Volatile oils** because they evaporate without decomposing, unlike fixed oils.
- **Ethereal oils** because they do not dissolve in water but dissolve in organic solvents such as ethanol and ether.

They are characterized by their high concentration, pungent odor, and easy volatility, as they evaporate completely without leaving a greasy residue. Essential oils dissolve in fats despite not containing fatty components, and their solubility in water is low. They are characterized by their small molecular size, which facilitates their absorption into the body whether applied to the skin or through inhalation. Once they enter the body, they begin to react in various ways depending on their type. They are also effective in disinfection and eliminating bacteria, especially Gram-positive bacteria, as they can penetrate the bacterial cell wall.

The term aromatherapy is derived from the words "aroma," meaning fragrance or scent, and "therapy," meaning treatment. This therapy, which is an integral part of herbalism (which itself uses all plants with medicinal properties), is a natural treatment method based on aromatic compounds extracted from plants. Medicinal essential oils are plant-derived oils with medicinal properties, as defined in the European Pharmacopoeia. An essential oil is an aromatic product, generally of complex composition, extracted from a specific botanical raw material, either by steam distillation, dry distillation, or an appropriate mechanical process without heating. The essential oil is most often separated from the aqueous phase by a physical process that does not significantly alter its composition.

Aromatherapy has been used for over 6000 years in many regions, including Egypt, China, India, the Middle East, Greece, the Americas, and Africa. However, this practice was abandoned in Europe during the Middle Ages. With the arrival of the Arabs, aromatic medicine revived and gained prominence in modern medicine. During the Industrial Revolution, the method of producing essential oils was discovered, allowing for the manufacture of new food products and perfumes. At the beginning of the 20th century, researchers discovered that essential oils have antiseptic and analgesic properties (lavender oil). Thus, in the 1930s, researchers coined the terms aromatherapy and herbalism to refer to medical practices using essential oils. As a result, the use of essential oils is increasing in the perfume, cosmetics, and pharmaceutical industries, as well as in food as flavorings.

.2. A long history of use

The oldest evidence of the use of essential oils dates back to the period from 3000 to 2500 BC, and it has been mentioned in the artifacts of several ancient civilizations, including:

Egypt: The ancient Pharaohs were known for their interest in cosmetics and medicine. Priests used plants and essential oils to make many medical prescriptions, ointments, and treatments. Women also used them for beauty care, and some Pharaonic recipes are still used today. Murals

in Pharaonic temples depict the extraction and use of essential oils. Researchers also found, upon the discovery of Tutankhamun's tomb in 1922, more than 50 vessels specially made for essential oils.

Greece: The Greek physician Hippocrates (the father of modern medicine) studied and documented the medical effects of more than 300 types of aromatic herbs. He was known to have used essential oil incense to purify the city during a plague outbreak, as well as using essential oils to treat wounded soldiers.

Rome: Roman culture was known to be influenced by Greek culture. The Greeks were known for their extravagant use of essential oils, and they mixed different types to make perfumes. One of the most important legacies they left in this regard is the book by the Greek physician Dioscorides, the Roman army physician, on the manufacture of medicines using aromatic plants and herbs, known as "On Medical Material." It was translated into Arabic as the "Book of Dioscorides on Simple Medicines." It is a five-volume encyclopedia, and after 1500 years, some of its recipes are still used today.

India: Essential oils are an essential part of Ayurveda, which in Sanskrit means "the science of life." It includes a medical treatment system practiced for nearly 5000 years and is still prevalent today in India and beyond. The Vedas, the sacred scriptures of Hinduism, mention more than 700 types of aromatic herbs and plants used for various religious and therapeutic purposes.

China: The Shennong Bencao Jing is one of the oldest medical texts that has come down to us, dating back to 2700 BC, and it included the use of 365 recipes extracted from plants. Traditional Chinese medicine has, for example, used lavender extract, from which lavandin is now extracted for the treatment of asthma.

.3. Uses of essential oils

You can use essential oils in several ways:

.3.1. Topical use

By diluting them in a carrier oil and using them for body massage. It is warned against using them directly without dilution in a carrier oil, as this may cause skin irritation. Suitable carrier oils include: coconut oil, avocado oil, grapeseed oil, sunflower oil, and almond oil. Method: For each teaspoon of carrier oil, add one drop of essential oil and mix well. This is the basic ratio, but proportions may vary from one essential oil to another.

.3.2. Diffusion in the air

Using a dedicated diffuser or humidifier, where water is placed with a few drops of essential oil, operating electrically, or using a traditional diffuser (without heat), where the essential oil is dispersed as small particles that are inhaled for the body's benefit and also freshens the air. Essential oils with pleasant scents that can be used this way include: peppermint, lavender, lemon, cedarwood, cinnamon, and lemongrass.

.3.3. Use of essential oils in agriculture

This is considered one of the modern methods of biological and environmentally friendly pest control in agriculture. Their most important uses include:

- Repelling harmful insects and attracting beneficial ones to flowers for pollination and reproduction.
- An energy element to facilitate chemical reactions.
- Maintaining adequate moisture for plant life in desert climates.
- Acting as repellent and lethal agents against insect pests, fungi, and bacteria that cause plant diseases, due to their content of toxins lethal to insects, microbes, and rodents.
- Examples include lemongrass, neem (*Azadirachta indica*), and citronella (*Cymbopogon citratus*).

.4. Most famous essential oils and precautions for their use

The list of essential oils can be long and seemingly endless; there are hundreds of them. Precautions for their use include:

- To maintain the effectiveness of essential oils, avoid exposing them to high heat or direct sunlight. Also, do not leave bottles open, as this leads to rapid oxidation.
- Do not apply essential oils directly to the skin without dilution, as this may cause skin irritation.
- Some oils are photosensitive; do not expose your skin to sunlight after applying essential oils, as this may cause burns, skin irritation, or discoloration.
- Keep essential oils out of the reach of children.
- Essential oils should not be used with children, pregnant women, or breastfeeding women unless it has been confirmed that this type of essential oil is suitable for their use, as some essential oils may be harmful to children or pregnant women.

- Most essential oils are not taken orally unless explicitly stated otherwise.
- Avoid getting oil into the eyes, nose, or ears.
- Some people are allergic to certain essential oils; perform a patch test on the inner arm before using the oil.
- Caution should be exercised when adding oils to bathwater, adhering to the dosages written on the package, as pores are open, increasing oil absorption.

Essential oils are one of nature's gifts, but we must ensure we use them correctly and appropriately so as not to lead to adverse results.

.5. Physical and chemical properties

- Essential oils are liquid at room temperature, except for camphor, which is solid.
- Most are colorless.
- Their density is often lower than that of water, except for sassafras, clove, and cinnamon.
- They have a high refractive index.
- They dissolve in alcohol, ether, and organic solvents.
- They are slightly soluble in water, but enough to give the water a distinctive fragrance, which is called aromatic water, such as orange blossom water and rose water.

.6. Chemical composition of essential oils

The chemical composition of essential oils varies depending on the region of growth and harvest, even if they are from the same plant species in some cases, as well as differences in extraction method, chemical analysis, and storage duration and conditions. Essential oils are also known as a mixture of complex compounds such as:

- Terpenoid compounds
- Aromatic compounds derived from phenylpropane
- Other various derived compounds

.6.1. Terpenoid compounds: Terpenoid compounds consist of multiple isoprene units (C5):

- Monoterpenes (C10)
- Sesquiterpenes (C15)
- Diterpenes (C20)

- Triterpenes (C30)

These are in the form of hydrocarbons or oxygenated derivatives.

.7. Methods of extracting essential oils

Among the most important traditional methods:

.7.1. Distillation

This process relies on the volatilization of essential oils by the action of heat, where they are carried by water vapor. As they pass through the condenser, the oil particles condense, and since the densities of water and oil are different, they are easily separated. This method is used to extract essential oils whose components are not affected by high temperatures.

.7.2. Water distillation

This method is used on plant material, whether leaves, flowers, or fruits. The oil components must not be affected by temperature. In this process, water is mixed with the plant material containing the oil to be extracted, and they are both subjected to heat until boiling. Water vapor is released carrying oil particles, which are then condensed and separated by density difference using a Clevenger apparatus.

.7.3. Steam distillation

This method is similar to water distillation, except that the water and plant material are placed separately. By the action of heat, steam passes through the plant from which the essential oil is to be extracted and carries it. Since the two liquids are immiscible, they are easily separated.

.7.4. Saturated steam distillation

This method is used on all plants that contain oils that can withstand high temperatures. The plant material is placed in mesh containers that allow steam to penetrate and extract the volatile oil, then carry it to the condenser where it is separated by density difference. (It is preferable to cut the plant into small pieces to collect the maximum amount of essential oil.)

.7.5. Cold pressing

The principle of this process is pressing or pricking, and it is specific to citrus fruits and essential oils that are affected by heat and which contain oil in special parts of the surface layer of the plant material's rind.

.7.6. Extraction with volatile organic solvents

This has great importance in the perfume industry, where the extracted oil is exactly identical to its state in the plant. This process is used to extract essential oils that are affected by heat and are present in small proportions in plant parts, such as jasmine oil and lily oil. The solvents are characterized by a low boiling point and easy separation of the volatile oil. The most important solvents include petroleum ether and hexane.

.7.7. Extraction with fats and oils

This method is used for valuable plants that are not affected by temperature, where the essential oil is found in the flowers. Various types of animal and vegetable fats are used. The extract is based on placing alternating layers of plant material and fatty substance, and the essential oil is collected in the fatty material because the compounds are soluble in fats, and they are separated using alcohol.

.7.8. Microwave extraction

This is one of the most important modern methods, primarily based on microwave radiation applied to plant powder in the presence of a solvent such as methanol for extracting polar compounds, and a solvent such as hexane for non-polar compounds. The mixture (plant material and solvent) is heated without reaching boiling point, connected to a condenser (cooling system), followed by a separation process.

.7.9. Supercritical carbon dioxide extraction

This is one of the newest and most effective extraction methods. It is used to obtain essential oils of high purity that are sensitive to temperature. Its advantage lies in the ability to work at low temperatures using supercritical carbon dioxide (between liquid and gaseous states).

The control of vector-borne diseases requires an integrated approach targeting both pathogens and vectors. Two integrated control methods are currently being developed:

1. Reducing the parasitic load through screening and/or diagnosis to apply appropriate treatment to infected individuals.

2. Reducing vector populations and limiting human-vector contact through vector control.

.8. Insecticidal efficacy of essential oils and plant extracts

8.1.Mechanisms of action

Essential oils represent a promising field for future research, and there are many studies conducted on oil extracts: the table prepared by Mohan and Ramaswamy (2007) (Appendix 1) summarizes the various studies and their results. However, the vast majority of these studies focused on mosquitoes, either on the repellent effect of essential oils or their larvicidal effect (Netunifor et al., 2006). The mechanism of action of essential oils in insects is still not well understood (Bekele and Hassanali, 2001) (Isman, 2000).

The use of synthetic insecticides, which are subject to increasing regulation to protect the environment, is a major cause of the emergence of many cases of insect resistance. In this context, the use of natural molecules (of ecological and economic importance) with insecticidal or repellent properties has proven its worth as an alternative to synthetic insecticides.

Plant extracts show larvicidal and adulticidal properties, as well as inhibiting oviposition in disease-carrying insects. Many types of extracts, depending on the solvents and plants used, cause high mortality rates in larvae and eggs, and inhibit oviposition in the following mosquito species: *Aedes aegypti*, *Anopheles gambiae* (sensu lato), *Culex quinquefasciatus*, and *Anopheles stephensi*. Extracts prepared by maceration in chloroform, hexane, ethyl acetate, and methanol show strong efficacy in killing larvae of *Anopheles gambiae*, *Aedes aegypti*, and *Culex quinquefasciatus*.

Numerous studies have shown the ovicidal, larvicidal, and adulticidal effects of essential oils against mosquitoes. Indeed, *Citrus hystrix*, *Citrus reticulata*, *Zingiber zerumbet*, *Kaempferia galanga*, and *Syzygium aromaticum* are plants whose essential oils have demonstrated primary larvicidal activity against *Aedes aegypti*. Larvae of *Aedes aegypti* and *Culex pipiens* are killed at low doses by oils from *Citrus bergamia*, *Bunium persicum*, *Pimenta racemosa*, *Psidium rotundatum*, and *Melaleuca leucadendron*, which cause 100% mortality at 25 ppm. Essential oils also exhibit knockdown and adulticidal activity against various mosquito species. Adulticidal activity against *Culex quinquefasciatus* has been demonstrated for *Lippia turbinata* and *Lippia polystachya* (Verbenaceae). The same applies to plants such as *Lantana camara*, *Schinus terebinthifolia*, and *Ocimum gratissimum*, whose essential oils are toxic to larvae and adults of *An. gambiae*, *Ae. aegypti*, *Cx. quinquefasciatus*, *An. culicifacies*, *An. pharoensis*, and *An. stephensi*.

Extracts prepared using solvents can show biological activity. Polar and non-polar solvents are used to extract active compounds against different stages of mosquito development. Studies

have shown that extracts prepared using benzene, ethyl acetate, acetone, hexane, chloroform, and methanol are ovicidal and larvicidal against various mosquito species. The larvicidal properties of extracts from 45 West African plants against *Anopheles gambiae* and *Culex quinquefasciatus* have been studied. Dihydronitidine alkaloids, caryophyllene oxide sesquiterpene, pellitorine amide, and sesamin extracted from *Zanthoxylum heitzii* are effective insecticides against adult and larval *Anopheles gambiae*. Aqueous extracts of neem also cause high larval mortality and inhibit the emergence of adult *Anopheles gambiae*.

Plant extracts in general, and essential oils in particular, do not generally stimulate the development of insect resistance to pesticides, thanks to their synergistic mechanism of action and the multiplicity of their target sites on the insect body. Studies have shown that some plant extracts are more toxic than organophosphate compounds to mosquito strains resistant to these pesticides, without leading to the emergence of resistance to these extracts. However, the mechanisms of action of plant extracts are still not fully understood. Some research has focused on the mechanism of action of some of these compounds, but other aspects still require further investigation. Some monoterpenes, such as eugenol, thymol, alpha-terpineol, terpinen-4-ol, 1,8-cineole, and linalool in essential oils, interfere with synaptic transmission, while other compounds, such as tannins, destroy the abdominal epithelium, the gastric caecum, and the Malpighian tubules of the insect showed that the essential oils of *Cymbopogon giganteus* Chiov., upon contact with *C. maculatus* and *C. subinnotatus*, stimulate an increase in acetylcholinesterase, glutathione S-transferase, and glutathione reductase enzymes in the bodies of these insects, indicating that these enzymes are the target sites for the essential oils.

Some polar plant extracts, specifically methanolic extracts, strongly inhibit the enzyme acetylcholinesterase. The variability in the sensitivity of the different mosquito strains tested during our study of the tested plant extracts justifies the interest in investigating the effect of these extracts (solvent extracts and essential oils) on acetylcholinesterase, one of the most important neurotransmitters in synaptic transmission in insects.

.8.2.The most effective examples, classified by their mode of action

1. Extracts with a direct lethal effect (Insecticides): These extracts contain molecules that attack the nervous or digestive systems of insects.

-Pyrethrum (extract of *Chrysanthemum cinerariifolium*)

One of the most potent. Its active ingredients (pyrethrins) attack the insects' nervous systems, causing immediate paralysis.

-Neem (extract of *Azadirachta indica*)

Neem oil or seed extract contains azadirachtin. This compound disrupts insect hormones, preventing them from feeding, maturing, and reproducing.

-Nicotine (extract of tobacco, *Nicotiana tabacum*)

A potent neurotoxin for insects. Note: Its use is now strictly regulated or banned in many countries due to its high overall toxicity.

2. Repellent and anti-feeding extracts: These plants do not kill directly but drive pests away or prevent them from feeding on crops.

-Chili Pepper (extract of Capsicum): Rich in capsaicin, this extract causes a burning sensation and effectively repels aphids, caterpillars, and mammalian pests.

- Garlic (extract of Allium sativum): Its sulfur compounds (such as allicin) act as a powerful broad-spectrum repellent against mites, aphids, and beetles.

-Citronella (extract of Cymbopogon): Rich in citronellal and geraniol, it disrupts the sensory receptors of flying insects (mosquitoes, flies).

3. Homemade preparations (Fermented plant extracts and macerations) : Widely used in organic farming and gardening, these plant extracts are obtained through fermentation in water.
- Nettle extract: At high concentrations or when lightly fermented, it acts as a repellent against aphids and spider mites (in addition to being an excellent fertilizer).

- Fern extract: Contains compounds toxic to insects' digestive systems; ideal for controlling wireworms or woolly aphids.

- Rhubarb maceration: Rhubarb leaves are rich in oxalic acid, a highly effective toxic repellent against aphids and leek moths.

-Geraniol

Geraniol is a volatile, fragrant molecule naturally found in plant-derived essential oils. Geraniol is particularly known for its larvicidal and ovicidal properties. It is an active substance used to formulate repellents and insecticides that are effective against a wide variety of insects and mites, such as: - Mosquitoes, houseflies, blowflies and other dipterans, wasps, hornets, -

Cockroaches, earwigs, crickets, ants, - Beetles, lepidopteran larvae, - Lice, fleas, dust mites, aphids.

Ticks and fleas …..etc…

Geraniol in aqueous solution acts on insects in two ways, regardless of their developmental stage (egg, larva, or adult): by suffocation and by dehydration through its effect on chitin (the insect's protective shell). Geraniol is one of the best larvicides and ovicides on the market. It is therefore used as a natural preventive measure against fleas and ticks on pets, to boost the insecticidal action of other products, or even as a repellent against blood-feeding insects—for instance, in the form of a protective wristband.

VII. Integrated control

Vector control methods can be integrated to combat multiple diseases simultaneously, as many of these methods are effective against a range of diseases. Consequently, the World Health Organization recommends Integrated Vector Management (IVM) as a process for developing and implementing vector control strategies. Integrated vector control relies on pooling resources and services across various levels and sectors to improve health outcomes. This integrated approach can be applied despite the differing natures of the diseases, as it capitalizes on the common elements of disease control. Conclusion Effective vector control programs are essential for preventing and controlling vector-borne diseases. By integrating strategies such as environmental management, biological and chemical controls, vaccination, and health education, we can significantly reduce the global burden of these diseases. Addressing challenges such as insecticide resistance, climate change, and resource constraints is key to the success of these programs, ensuring public health, and saving lives.

Vector control methods can be integrated to combat multiple diseases simultaneously. Many of these methods are effective against multiple diseases; therefore, the World Health Organization recommends Integrated Vector Management (IVM) as a process for developing and implementing vector control strategies. Integrated vector control relies on pooling resources and services across various levels and sectors to improve health outcomes. This integrated approach can be applied despite the differing natures of the diseases, as it capitalizes on the common elements of disease control.

In conclusion Effective vector control programs are essential for preventing and controlling vector-borne diseases. By integrating strategies such as environmental management, biological and chemical controls, vaccination, and health education, we can significantly reduce the global burden of these diseases. Addressing challenges—such as insecticide resistance, climate change, and resource constraints—is key to the success of these programs, ensuring public health, and saving lives.

Communicable diseases remain at the forefront of public health problems, despite the availability of successful health measures. This is especially true in countries suffering from poverty, civil wars, and disasters. The main reason why control efforts have not achieved better results is the limited availability of financial and human resources.

Integrated vector control is based on integrating resources and services at various levels and in most sectors, with the aim of improving health outcomes. The integrated approach can be applied even when the nature of diseases differs, as it combines the common aspects of disease control.

Integrated control ensures greater equity in the distribution of health resources and guarantees their optimal use, in order to alleviate the burden of disease and the suffering of populations, as well as being consistent with building a health system based on primary health care.

.1. Components of a vector-borne disease control program

.1.1. Integrated Vector Management (IVM)

Integrated Vector Management (IVM) combines several methods to control vector populations, ensuring an effective reduction in disease transmission.

- **Environmental management**
- Modifying ecosystems to reduce breeding sites, such as draining standing water.
- **Biological control**
- Introducing natural predators or using pathogens to target vectors.
- **Chemical pest control**
- Using insecticides to reduce vector density.
- **Personal protection**
- Using insecticide-treated nets and insect repellents.

.2.1. Legislation and policy

Implementing policies that support vector control initiatives.

.2. Surveillance

Surveillance of vector populations and tracking of disease cases are essential for the success of a vector control program. Regular data collection allows for the identification of targets and the effective allocation of resources in the most vulnerable areas.

.3. Community participation

Involving the local community ensures the success of vector control efforts. Educating the public about the risks of vector-borne diseases and prevention strategies encourages participation, such as eliminating mosquito breeding sites.

.4. Vector (mosquito) control strategies

Mosquitoes are the main vectors of diseases such as dengue fever, malaria, and Zika virus. Implementing targeted strategies can significantly reduce mosquito populations. Source on interior surfaces kills mosquitoes. Insecticide-treated nets provide personal protection against bites. Biological control provides natural predators and bacterial treatments as effective alternatives to chemical interventions. Genetic control uses advanced techniques such as genetic modification to reduce mosquito populations and disease transmission, including the sterile insect technique (SIT) by releasing sterile male mosquitoes to reduce breeding populations, and gene drive technology by introducing genetic traits that reduce vector competence.

The prevention and control of vector-borne diseases also rely on:reduction, i.e., managing and eliminating mosquito breeding sites, is crucial for their control. Environmental management includes removing standing water, maintaining environmental cleanliness, improving waste disposal, and larviciding using larvicides in water sources to kill mosquito larvae before they mature. Additionally, indoor residual spraying (IRS) of insecticides

- **Vaccination**
- An essential tool in preventing diseases such as dengue fever, where a vaccine exists that reduces its incidence in affected populations.
- **Personal protection measures against mosquito bites**
- Essential in areas at risk of vector-borne diseases, including the use of insect repellents and protective clothing (long sleeves and long pants) to reduce skin exposure.
- **Awareness raising (health education)**
- About vector-borne diseases encourages individuals to take preventive actions, such as eliminating breeding sites and using protective measures.
- **Environmental management in vector control**
- Including water management, waste management, urban planning, and integrating chemical, biological, and environmental strategies to combat resistance.
- **Climate trend monitoring and adaptive management:** Adjusting vector control programs based on evolving climate data.

- **Staff training and infrastructure building**
- To ensure long-term sustainability of vector control.
- **Collaboration with partners**
- To share resources and expertise to significantly reduce the global burden of these diseases.

Addressing challenges such as insecticide resistance, climate change, and resource constraints is key to the success of these programs, ensuring public health and saving lives.

Vector control methods can be integrated together to control multiple diseases simultaneously, as many of these methods are effective against multiple diseases. Integrated vector control is based on integrating resources and services at various levels and in most sectors, with the aim of improving health outcomes. The integrated approach can be applied even when the nature of diseases differs, as it combines the common aspects of disease control. Therefore, the World Health Organization recommends Integrated Vector Management as a process for developing and implementing strategies for vector control.

Effective vector control programs are essential for the prevention and control of vector-borne diseases. By integrating strategies such as environmental management, biological and chemical controls, vaccination, and health education, we can significantly reduce the global burden of these diseases. The World Health Organization has warned that more than 80% of the world's population is at risk of vector-borne diseases, necessitating the adoption of sustainable control strategies that adapt to environmental changes.

Perspectives

The face of our world is changing rapidly, at a pace far more intense than in past centuries. Deforestation, coupled with the exploitation of tropical forests in Africa, Asia, and the Americas for over a century, facilitates the spillover of pathogens from their sylvatic transmission cycles. Between rampant urbanization—which will see five billion of our fellow citizens living in cities by 2030, likely increasing contact between humans and urban mosquitoes—and human-induced climate change—which is causing global warming of the biosphere and intensifying extreme weather events (droughts, floods, etc.)—there is no doubt that the mosquito, an unrivaled champion of adaptation, will find the means to acclimatize to these new environmental conditions. Such conditions could lead to a significant risk of invasion by new mosquito species or the re-emergence of pathogens. Regarding human societies, however, there is far greater uncertainty concerning their capacity for change and adaptation. Does this mean, then, that the mosquito will emerge victorious from this long-standing confrontation with humanity? The single-track strategy long championed—relying heavily on biocides to combat mosquitoes—has revealed its flaws: ecological imbalances and the emergence of resistance that undermines control efforts, compounded by issues regarding the environmental persistence or toxicity of the chemical agents used. We now possess a wealth of knowledge regarding the bioecology and vector competence of various mosquito species; this knowledge can be leveraged to craft tailored vector control strategies suited to local conditions (environment, climate, etc.), human communities, and public perceptions of control measures. Let us prepare for the inevitable by investing time and resources in developing new vector control tools, as these often remain our only defense against vector-borne diseases. It is time to adopt innovative control strategies that are environmentally friendly and fully accepted by the affected populations.

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