Canadian Association of Physicians for the Environment

Backgrounder: Pyrethroids — just because we can use them at home doesn't mean that they're harmless

During the Napoleonic wars, extracts of chrysanthemum flowers (Figure 1) were renowned for their ability to kill insects. These extracts–known as pyrethrum–provided soldiers relief from lice.[1, 2] The insecticidal activity of natural extracts was fleeting, however, so chemists modified their structures to make them more effective and persistent. This is when pyrethroids were born as a class of insecticides. Today, approximately 614 pesticides containing pyrethroids are registered in Canada[3] and more than 3,500 in the USA.[4]

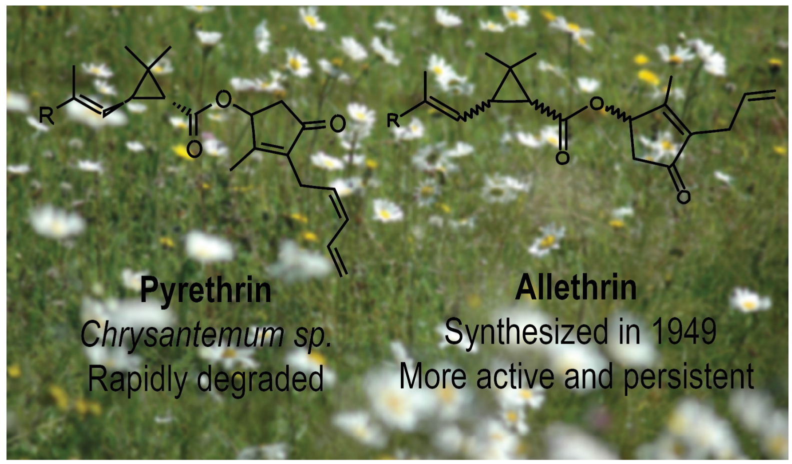

Figure 1: Comparison of pyrethrin, extracted from chrysanthemum flowers, and allethrin, the first synthesized pyrethroid.

Pyrethroids are increasingly used (Figure 2) to replace organophosphates–a family of insecticides considered to be more toxic. Today, pyrethroids dominate the global insecticide market, with a 17% market share and an estimated market value of $7 billion.[5] Pyrethroids include familiar brands such as Raid or OFF! products. In Québec, they are the class of insecticides most widely used by professional exterminators, and their domestic use doubled from 2004 to 2010.[6] They are also widely used for veterinary or medical applications,[7] such as in lice and flea shampoos. Some pyrethroids are currently undergoing re-evaluation by the Pest Management Regulatory Agency (PMRA), within Health Canada.[8]

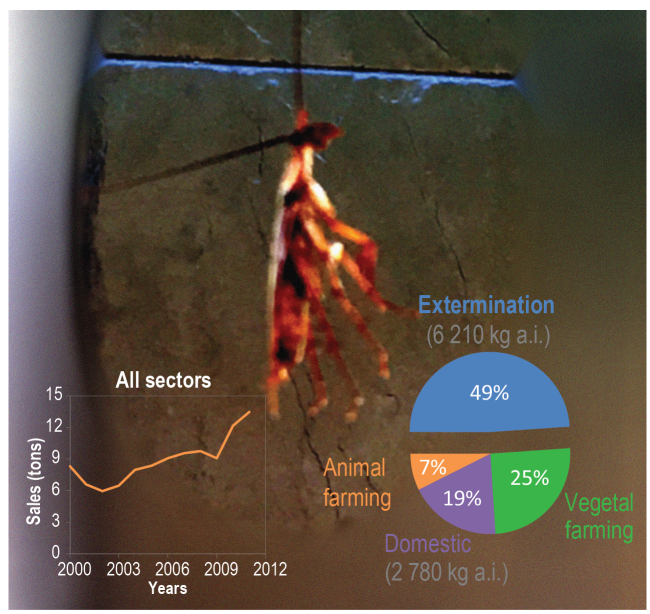

Figure 2: Pyrethroids sales in Québec.

How pyrethoids work

Pyrethroids are powerful insecticides that rapidly immobilize and paralyze targeted insects.[9] Pyrethroids are neurotoxins, which interfere with the messages sent along nerves (by maintaining sodium channels in an open position, they allow repetitive nervous influx, or a depolarization, which leads to different symptoms such as tremors, involuntary movements and enhanced salivation in animals, Figure 3). In addition to their active ingredients, formulations sold on the market may also contain one of two common co-formulants that enhance the toxicity of pyrethroids.[4] These synergists, piperonyl butoxide and MGK-264, inhibit enzymes that break down pyrethroids, making them last longer; they are also toxic themselves.[4]

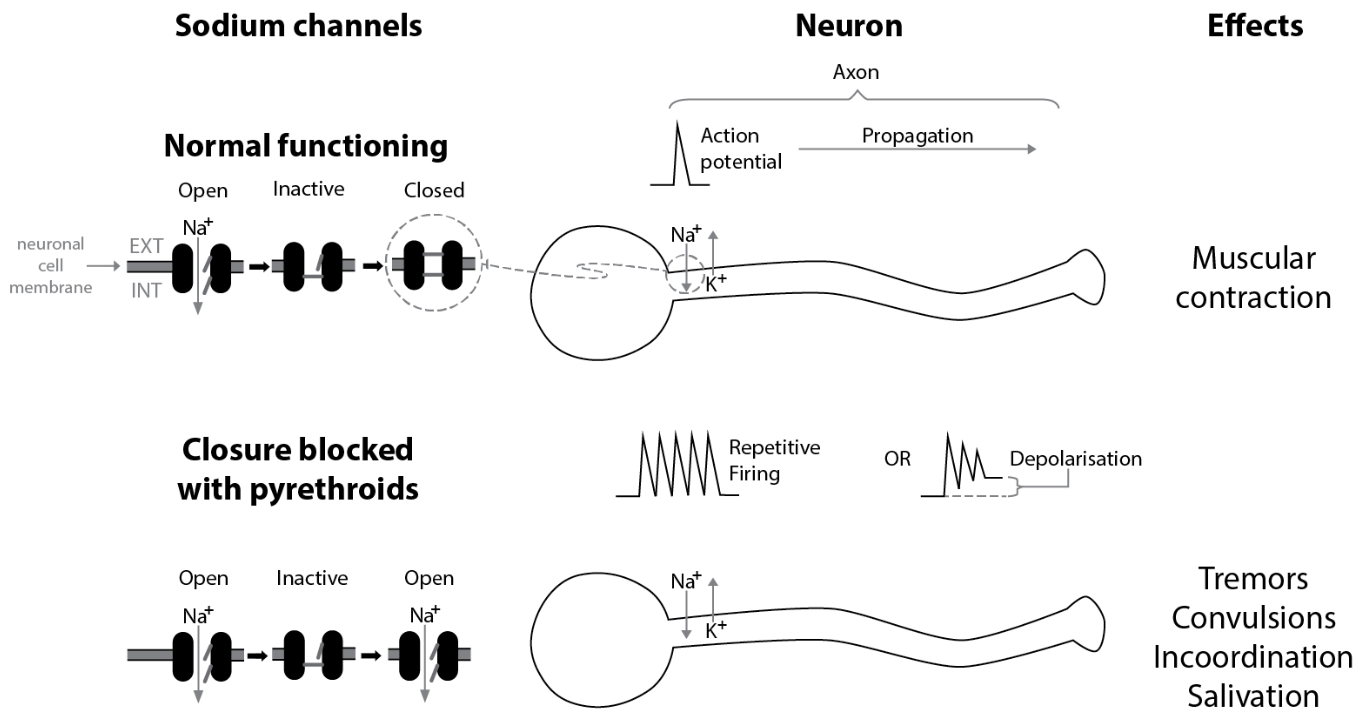

Figure 3: Pyrethroids' mode of action on neurons.

Pyrethroids are commonly used in homes and on food

Pyrethroids are often used against flying or crawling insects or other bugs: in homes for cockroaches, wasps, ants and spiders; animal parasites such as fleas and ticks; and lice on humans (Figure 4). They are also used to control mosquitoes in areas where they may be carrying infectious diseases such as West Nile Virus. They are used to fight agricultural pests such as aphids and weevils on crops and flies on livestock. In addition, pyrethroids registered in Canada (or pyrethroids registered in foreign countries from which food is imported) are used on fruits such as apples, strawberries and other berries, and vegetables such as sweet corn, potatoes, carrots, lettuce, onions, chives and cruciferous vegetables.[7, 10, 11] Pyrethroids can be delivered in many different forms: in powders, gels, traps, spray solutions, combustible spirals, and in aerosols delivered from spray cans and bombs.[12] The greatest risk of poisoning occurs when they are delivered in a mist or smoke.[13]

Not persistent, but omnipresent

Natural pyrethrins are rapidly degraded in the presence of humidity by sunlight or microorganisms.[14] Synthetic pyrethroids, however, are more stable. Inside homes,[15] protected from the elements, pyrethroids may be even more persistent. In domestic use, they may be disposed of through sewers and water treatment plants which are ineffective at removing the chemicals.[16] In outdoor applications, pyrethroids can enter surface waters when washed off surfaces by rain,[10, 17] particularly in urban areas where they are used near to, or on, impervious surfaces that facilitate runoff (Figure 4).[18]

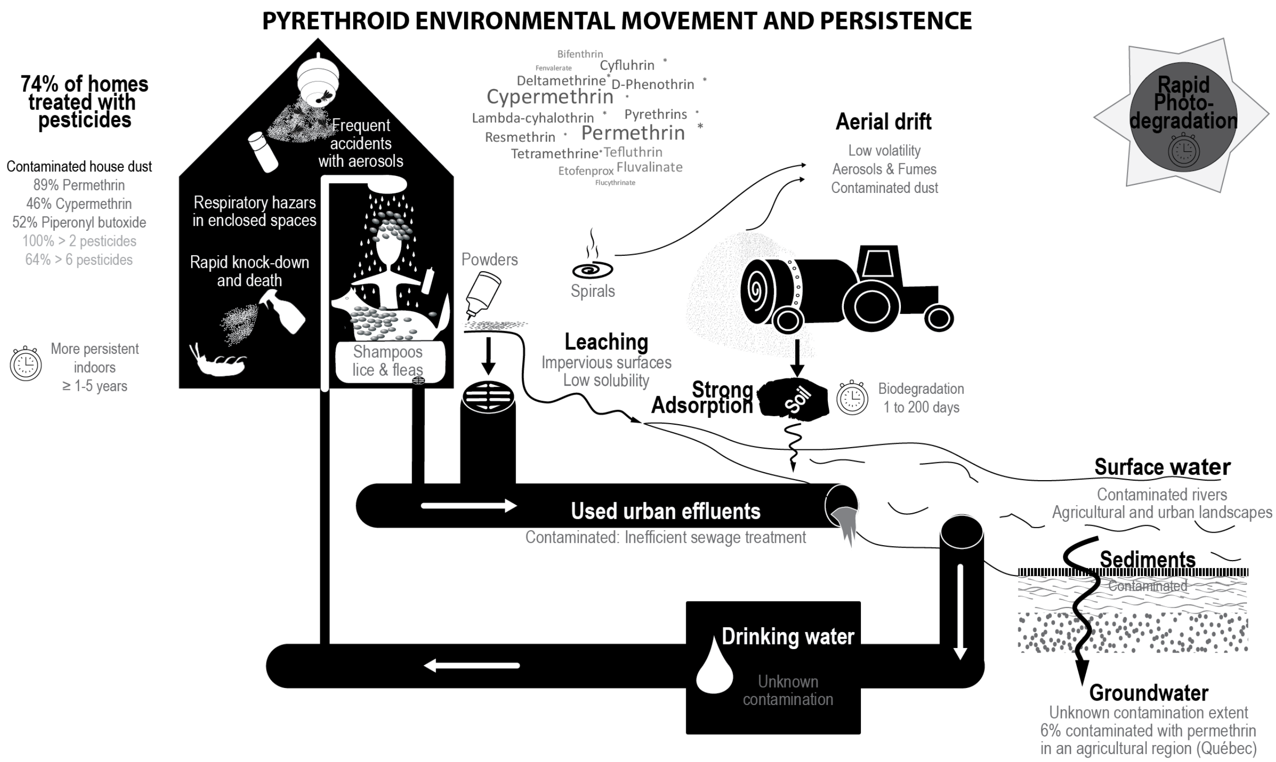

Figure 4: Transport and persistence of pyrethroids within buildings and in the outside environment.

Surface waters of certain agricultural regions of Québec have detectable levels of pyrethroids (i.e., permethrin, cypermethrin, lambda-cyhalothrin)[10, 19] in concentrations which may surpass the criteria established to protect aquatic life.[10] According to an American study, urban surface waters may be even more contaminated by pyrethroids than are agricultural waters.[18] Permethrin and piperonyl butoxide, common pyrethroids formulation ingredients, have also been found in Québec aquifers.[20] Although 20% of Québec residents–scattered over 90% of the inhabited territory–drink groundwater, our knowledge of pyrethroid concentrations in groundwaters remains fragmentary.[21]

The general human population is mainly exposed through food or water, while workers are exposed by inhalation and skin contact

People are most frequently exposed to pyrethroids by ingesting contaminated food or water.[1] Unfortunately, pesticide residues are not completely removed from fruits and vegetables by dipping them in water.[22] Little is known about the levels of pyrethroids in drinking water, since pyrethroids are not among the 31 pesticides which must be tested in large Québec municipalities.[23] However, pyrethroids have been detected in surface waters in the fruit and vegetable growing regions of Québec.[10, 19] Furthermore, permethrin and an additive used in pyrethroids formulation (piperonyl butoxide) have been detected in ground water in one region of Québec at a frequency and concentrations which suggest the need for systematic monitoring.[20]

According to an American study, dust from the majority of homes contains measurable levels of pyrethroids or other ingredients added to pyrethroid-based insecticides.[24, 25] Because we spend up to 90% of our time indoors, should we worry that 74% of homes may have been treated with different pesticides, including pyrethroids?[12] Pyrethroids can be absorbed through the skin during application or upon contact with treated surfaces, because pyrethroids are fat soluble.[1] Fine droplets or suspended dust particles in the air can also be inhaled, especially when pyrethroids are used in confined spaces.[1, 26] Workers in the pesticide industry, exterminators and farmers can be exposed through inhalation and absorption through their skins.[27]

Children are especially at risk of exposure and intoxication

Food items regularly consumed by children are not systematically, nor regularly, tested for pesticides,[28, 29] but one American study found pyrethroids in 5% of food items regularly consumed by children.[28] Most children's exposure occurs through their diet, but they can also be exposed to pyrethroids by inadvertently ingesting contaminated soil and dust,[1] eating food that has fallen on the ground,[30] or by absorption through their skin.[31] Children tend to be more sensitive to pesticides than adults and they are more at risk of long-term harm because their bodies are still developing.[a] [27, 32-35]

Certain risks associated with domestic use of pyrethroids

Pyrethroids are sometimes used to control pests which present health hazards. For instance, cockroaches are known to trigger asthma attacks in sensitive patients. However, insecticides can present a health hazard as well. For instance, pyrethroids may also trigger asthma in sensitive humans.[36] Asthma attacks linked to pyrethroid use may be fatal. For example, one child in the US died from an asthma attack after treating her dog for fleas with a pyrethrin shampoo.[13, 37] Because pyrethroids can control both fleas and lice, parents noticing that animal flea shampoos have similar active ingredients were found to have treated head lice in children with shampoo destined for pets, as a means to lower the costs of treatments, without consideration that this usage represents a risk not-evaluated by the PMRA. This potentially dangerous behaviour, which goes against pesticide label instructions, should be prevented. The fatality suggests that consumers may not always read or follow warning labels, possibly due to lack of understanding of the risks associated with the use of pesticides. In addition, repeated pyrethroid treatments for lice have been shown to lead to resistance in target pest populations. In these cases, increased doses of pyrethroids or combinations with other insecticides may be necessary to circumvent resistance.[38] Yet at the same time, some specialists question the necessity of using any chemical

[a] Children may be more sensitive to pyrethroids than adults because they have a smaller body weight, breathe and eat proportionally more, play more often on the ground and have an increased propensity for hand-to-mouth behaviour. In addition, their detoxification system may not be fully mature, and their rapid development may give rise to particular windows of sensitivity, for example, during brain development.

insecticides at all to treat head lice.[39] They believe that fine combing and nit picking, along with attentive surveillance, may be sufficient.

Reversible Short-Term Acute Poisoning Symptoms, But Poorly Characterized and Worrisome Long-Term Effects

Short-term symptoms of pyrethroid exposure (Figure 5) inferred from animal studies include fine tremors, salivation and choreoathetosis (irregular muscle contraction).[40] Abnormal facial sensations (paresthesia) have been reported in exposed workers.[41] Non-specific symptoms of pyrethroid exposure have also been reported. These include nausea, dizziness, headache, fatigue, palpitations, chest tightness, blurred vision, difficulties breathing, skin rashes, memory loss, and changes in the immune system.[41, 42,26] The fact that these symptoms may occur for various reasons makes them difficult to link to a unique cause.[26, 43] While the effects of short-term exposure to pyrethroids are well-documented, the effects of long-term exposure to pyrethroids are not as well known, and the scarcity of epidemiological studies in humans may explain our lack of knowledge.[27] Furthermore, short-term symptoms often disappear within 12 to 48 hours, because pyrethroids are rapidly metabolized and excreted from the body,[44] making long-term studies of side-effects challenging. Sublethal effects (which do not kill the exposed organism) that result from long-term exposure in animals are varied.[27, 45] In general, concerns have been raised about the potential adverse effects of pyrethroids on the nervous system,[46] neurodevelopment,[44, 47, 48] the reproductive system,[27, 36, 49, 50] and the endocrine system (Figure 5).[27, 51-56,27, 57-59]

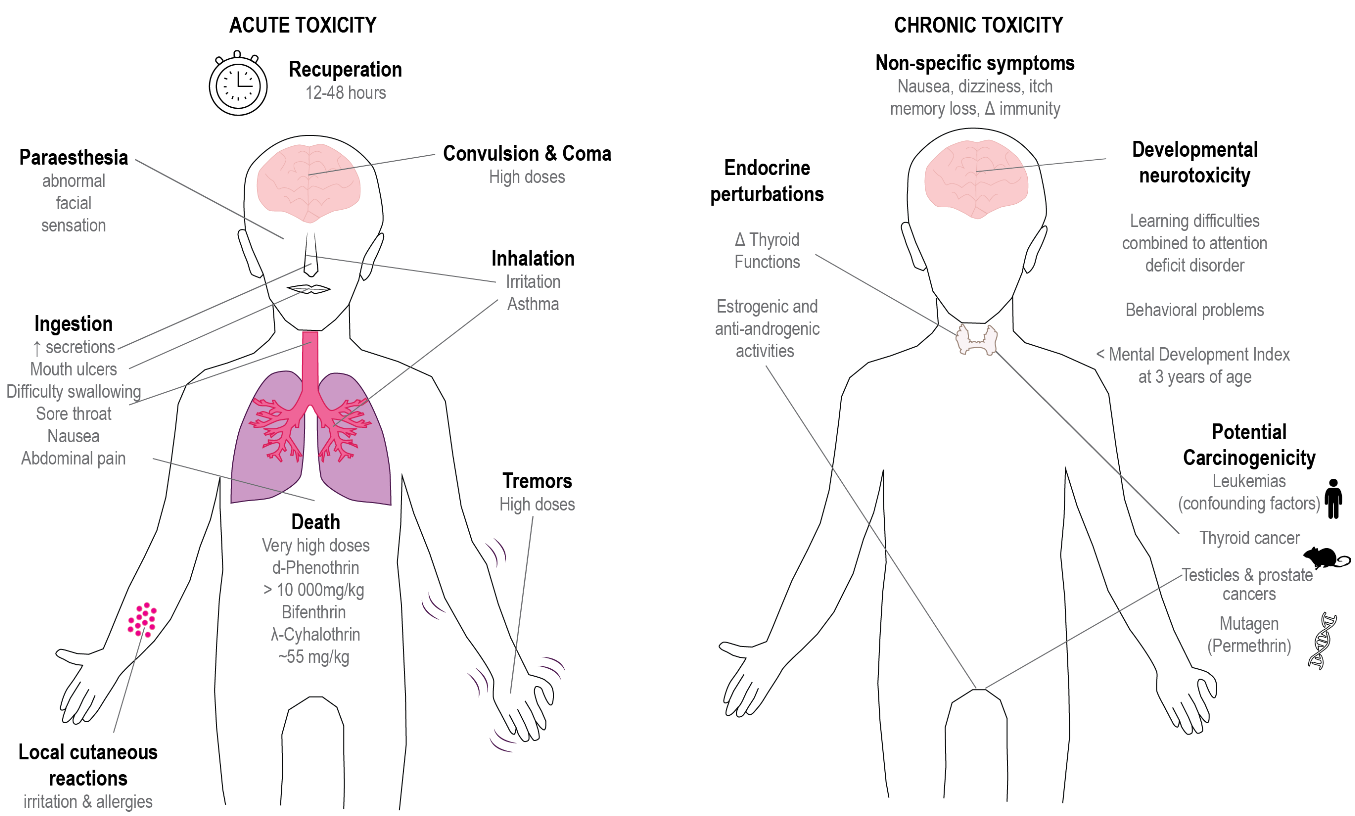

Figure 5: Acute and chronic effects of pyrethroids.

Neurodevelopmental Effects in Children

A comprehensive literature review categorized pyrethroids as substances toxic to the developing nervous system.[47] Some pyrethroids are toxic to cells involved in the development and maintenance of the brain,[47, 60] which could explain the greater sensitivity of newborn rodents compared to adult rodents.[47,44,46]

A study conducted at the Columbia Centre for Children's Environmental Health on 230 New York City children found that children with the highest exposure to piperonyl butoxide (one of the additives used with pyethroids) scored 3.9 points lower on the mental development index scale (normal scores were above 85).[61] One epidemiological study found an association between the pyrethroid bifenthrin and autism spectrum disorder in children.[62] Another found that children with the highest concentrations of pyrethroid metabolites in their urine had a greater risk of developing behavioural problems and/or learning difficulties combined with attention deficit disorder.[63] One Canadian study found that 97% of children have at least one detectable pyrethroid metabolite in their urine, and higher concentrations are associated with an increased risk of behavioural problems as reported based on parental assessment.[34] Based on animal studies, juvenile exposure can lead to persistent effects in adulthood.[48]

Human Fertility May Be Affected Via Hormonal Perturbations

Both animal laboratory studies and human epidemiological studies have suggested potential effects of chronic pyrethroid exposure on fertility. These effects include modifications to the male reproductive system, decreased sperm count and sperm mobility, and DNA damage, all of which could lead to reduced fertility and decreased pregnancy rates. [27, 49, 50]

Pyrethroids are endocrine disruptors, decreasing testosterone levels (male hormone), interfering with luteinizing hormone[51,56] (a hormone involved in spermatogenesis and ovogenesis), and altering thyroid function.[57-59] Laboratory animal studies or cell-line culture (*in vitro*) studies using the pyrethroids cypermethrin and fenvalerate demonstrated that some pyrethroids can modify secretion of certain male and female hormones (estrogenic and antiandrogenic effects).[51-54]

Pyrethroids May Be Carcinogenic

The pyrethroid permethrin has been shown to induce mutations in hamster and human cell lines.[51] The US Agency for Toxic Substances and Disease Registry (ATSDR) has classified the three pyrethroids, deltamethrin, fenvalerate and permethrin, as possible human carcinogens.[1] Recently, the International Agency for Research on Cancer (IARC) considered an updated review of permethrin's carcinogenicity to be a high priority for the 2015-2019 period.

Pest Insects Are Not the Sole Victims of Pyrethroids

Certain beneficial insects (Figure 6), such as bees, can be killed or sub-lethally affected by pyrethroids[14, 64] when exposed during the application process or when they visit treated plants.[65] Sublethal concentrations of insecticides, including pyrethroids, are suspected of contributing to the worldwide decline of bee populations, in combination with other environmental factors.[64, 66] Other invertebrates, such as earthworms who play a crucial role in organic matter recycling,[67] can also die or suffer sublethal effects from long-term exposure to pyrethroids.[68]

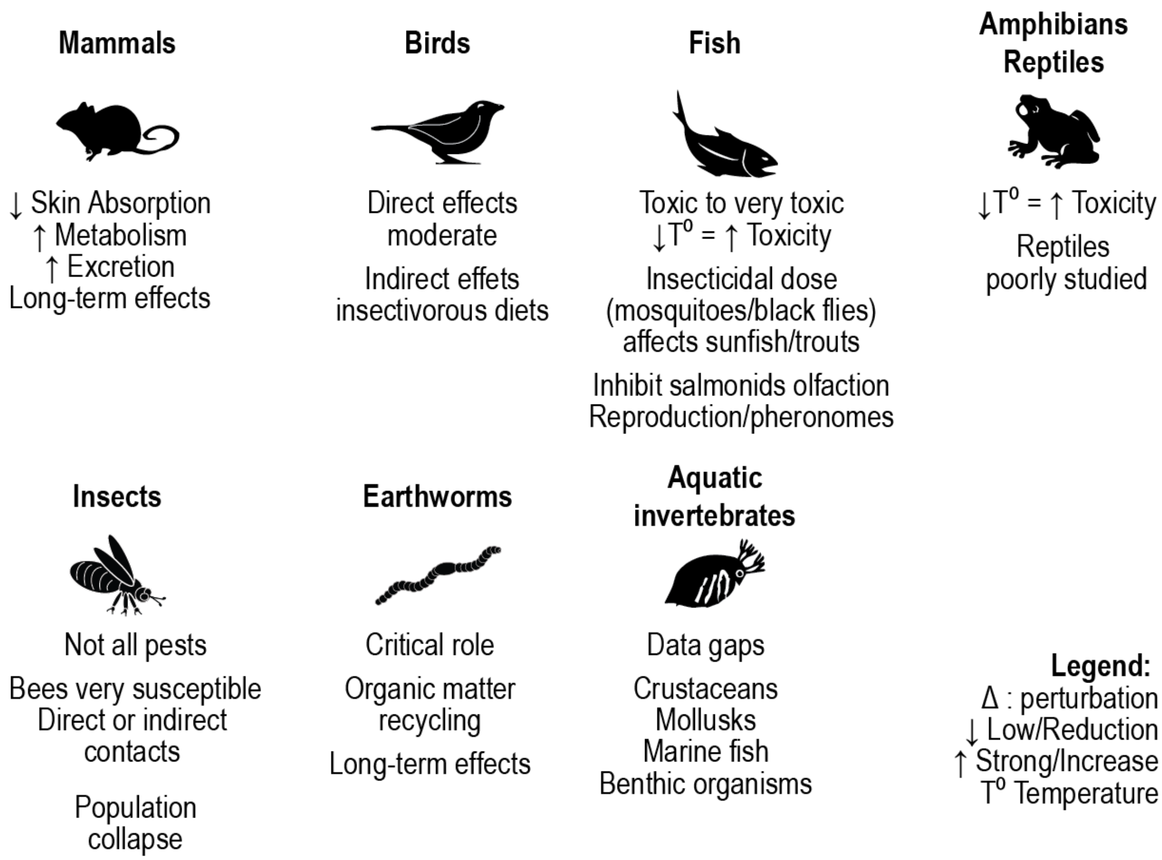

Figure 6: Pyrethroids' ecotoxicology.

Even if as little as 1% of the applied pyrethroids reach surface water bodies, this quantity suffices to harm aquatic organisms.[17] All tested pyrethroids are toxic, or highly toxic, to fish.[14, 69] Unfortunately, toxicity evaluations for crustaceans, mollusks, marine and estuarine fish, as well as benthic organisms, are severely limited.[70, 71] Fishes and frogs[69] (also reptiles[72]), are more sensitive to pyrethroids at lower temperatures.

Though mammals are sensitive to long-term exposure to pyrethroids, they are relatively well protected from them because of slow absorption through the skin, rapid metabolism and metabolite excretion.[41] However, co-formulants like piperonyl butoxide slow the metabolism of pyrethroids. Furthermore, detoxification capabilities may vary between individuals, leaving some at higher risks. It is assumed that birds are only moderately sensitive to pyrethroids, but this assumption does not take into consideration the indirect effects of reduced insect availability in their diets in areas where pyrethroids are used.[73] The toxicity for reptiles is rarely studied for registration purposes.[74]

Environmental Mixtures Represent a Poorly Assessed Risk

In Canada and the USA, surface waters and sediments in agricultural or urban regions contain pesticide mixtures that include several pyrethroids.[18, 19] Research has demonstrated that, together, organophosphorus compounds and pyrethroids can increase toxicity to fish by 140-170% (meaning that both compounds together are far more toxic than the sum of the toxicity of each compound administered in isolation) due to inhibition of metabolic pathways normally involved with detoxification by organophorphorus compounds.[75] Furthermore, each insecticide affects the nervous system differently (pyrethroids along the axon, and organophosphorus at the synapse). Synergistic toxicity of pyrethroids and neonicotinoid pesticides, often found in Québec surface waters, has also been reported for bees.[19] House dust is also a complex mixture of pesticides: 64% of kitchen floor wipes contains six different pesticides simultaneously.[12] Such combinations can arise accidentally, but also deliberately, for instance when organophosphorus insecticides are mixed with pyrethroids to treat insects with evolved resistance to either substance.[76] Epidemiological data suggest that this combination can reduce the number of spermatozoids in humans.[76] Further research on the environmental and human health impacts of intentional or unintentional mixtures of pesticides is necessary.[76]

Regulatory Reviews Are Underway

Several pyrethroids are currently under registration review in Canada[8] and the USA,[4] with decisions expected in 2016.[8] It is worrisome that pyrethroids–with a primary insecticidal mode of action to disrupt neurons and which exhibit adverse effects on neurotransmitters or receptors that induce behavioural changes–are not required to undergo mandatory advanced neurotoxicity testing in the registration process.[4, 9, 44] In Québec, the Drinking Water Regulation (*Règlement sur la qualité de l'eau potable*) originating from the Environmental Protection Act (*Loi sur la protection de l'environnement*), requires regular monitoring of pesticides in drinking water treatment plants serving more than 5,000 people, but pyrethroids are currently excluded from this monitoring requirement. In 2003, the Pesticide Management Code (*Code de gestion des pesticides*), a regulation under the Pesticide Act (*Loi sur les pesticides*) of Québec, was adopted.[77] Although the Code is intended to mitigate the health and environmental impacts of pesticides, it does not restrict pyrethroid use, except in places commonly frequented by children (daycares, elementary and secondary schools).[78] The environmental impacts index associated with pyrethroid uses in Québec agricultural regions has increased in the recent years, which goes against policy goals.[6]

Alternatives to Pyrethroids

Several alternatives to pyrethroids exist. They include physical, biological or less toxic chemical treatments. For example: heat can kill bed bugs and head lice; and cold can kill bed bugs, head lice and cockroaches.[78-83] Regular monitoring, early intervention, sometimes with the assistance of a professional exterminator or health practitioner, can increase the effectiveness of non-chemical alternatives to pyrethroids. Combing (repeated on days 1, 5, 9 and 13) can even be more effective than certain lice-shampoo treatments.[39] In agriculture, biological insect control may be used. This involves using a pest insect predator or parasite to control pest populations.

Conclusion

Toxicity evidence from laboratory animal studies and human epidemiological studies indicates that pyrethroids are developmental neurotoxins that may also adversely affect behaviour, fertility, hormonal balance and possibly induce cancer. Based on recently acquired knowledge concerning the health and environmental risks of pyrethroids, in January 2016, groups such as Équiterre began to pressure the governments of Québec and Canada to prohibit domestic uses of pyrethroids and to restrict their agricultural uses.

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