INSECTS AND DISEASE IN THE 21ST CENTURY
– A WIND OF CHANGE –

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Dedicated to the memory of Chris Curtis, who was at the forefront of modern malaria control

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Mr. Rector, ladies and gentlemen,

Infectious diseases of humans and animals associated with arthropod vectors continue to catch the limelight of the international press, mostly because they are the cause of great unrest and suffering among people across the globe. Although many of these diseases are endemic in least developed countries in the tropics, several of them are highly prevalent in our own country or threaten to invade as a result of trade, traffic and climate change. My story, therefore, could be one of misery and horror. I will, however, demonstrate how through collective knowledge, innovative collaborative research programmes and national and international initiatives, important steps have been taken that provide a hopeful perspective such that these diseases may be brought under control, or perhaps even be eradicated.

Arthropods are a fascinating group of organisms: many have complex biologies with beneficial traits, such as the honeybee, which is responsible for the fertilization of thousands of plants and, in the process, produces honey and wax, both important commodities for mankind. Another example is parasitic wasps, which act as effective natural enemies of herbivorous pests in forestry and agriculture. In the same light, ants are an often-forgotten group of beneficial insects that have an important role in the food web in a wide range of ecosystems. Sometimes, however, bees and ants are viewed as harmful because of their painful stings. In this way, these insects enter the world of public health, which is the subject of this lecture. They provide important ecological services to humans.

Arthropods form an important part of the world's biomass and they contribute significantly to the rich biodiversity of species. Many higher organisms would starve without them. For these reasons, arthropods are considered essential for life on earth as we know it.

A relatively small, but very important group of arthropods, however, has become infamous. These include arthropods that parasitize higher vertebrates or act as carriers of pathogens and parasites. I will name a few, several of which are well known because of their historic reputation among travellers: tsetse flies are the vectors of African sleeping sickness and animal trypanosomiasis, a major hindrance to agricultural development in Africa; anopheline mosquitoes act as vectors of malaria, but also of lymphatic filariasis and sometimes, arboviral diseases; yellow fever mosquitoes are responsible for the transmission of yellow fever, but also of dengue virus, Chikungunya virus and other arbo-viruses; rat fleas are the vectors of bubonic plague, which wiped out one third of the population of Europe in the Middle Ages; and body lice act as the principle vectors of typhus, a disease by which more soldiers were killed than by fighting during the First World War (Mullen and Durden 2002) (Table 1).

Table 1 – Examples of prevalent vector-borne diseases and arthropod pests affecting human and animal health, their vectors, distribution and current prevalence and epidemiological status (modified after Takken & Knols 2007).

	Arthropod vector or pest	Common distribution	Prevalence (epidemiological status)
Disease			
Malaria	*Anopheles* spp.	Tropics	++++
Leishmaniasis	*Phlebotomus* spp.	Tropics, southern Eu	+++
Trypanosomiasis	*Glossina* spp.	Tropical Afr	+++
Chagas disease	Triatominae	Tropical Am	++
Babesia	Ixodidae spp.	Global	+++
Onchocerciasis	*Simulium* spp.	Afr, tropical Am	++
Filariasis	*Culex quinquefasciatus*, *Anopheles* spp.	(Sub)tropics	++
Dengue	*Aedes aegypti*	(Sub)tropics	++++
Chikungunya	*Aedes aegypti* & *Ae. albopictus**	Afr, Asia, (Eu)	+ (emerging)
Japanese encephalitis	*Culex tritaeniorhynchus*	Asia	++
West Nile	*Culex pipiens*	Afr, ME, Eu, Am	++ (emerging)

other arboviruses*	Mosquitoes, ticks	Regionally prevalent	+, ++ (emerging)
Typhus	*Pediculus humanus*	(Sub)tropics	+
Plague	Flea	Global, sporadic	+ (sporadic)
Bartonella quintana	*Ixodes ricinus* / *Pediculus humanus*	Global	+ (emerging)
East coast fever	*Rhipicephalus appendiculatus*	Afr	++
Q-fever	Ixodidae spp.	Global	+ (emerging)
Human granulocytic ehrlichiosis (HGE)	*Ixodes* spp.	Northern hemisphere	+
Lyme disease	*Ixodes* spp.	Northern hemisphere	+++
Rickettsia helvetica	*Ixodes ricinus*	Eu	+
Tick-borne encephalitis	*Ixodes ricinus*	Eu	+++
Tularaemia	*Ixodes ricinus*	Northern hemisphere	++
Bluetongue	*Culicoides* spp.	Afr, Asia, Au, Eu, Am	+++ (emerging)
African horse sickness	*Culicoides* spp.	Afr, (Eu)	++
Pests			
Head louse	*Pediculus humanus capitis*	Global	++
Bedbug	*Cimex lectularius*	Global	+ (emerging)
House fly	*Musca domestica*	Global	++
Asian tiger mosquito	*Aedes albopictus*	Asia, southern Eu, Afr, Am	+ to +++ (emerging)
Sheep blowfly	*Lucilia sericata*, *L. cuprina*	Au, Asia, Eu	++
Sheep scab	*Psoroptes ovis*	Northern hemisphere	++

Afr = Africa; Am = Americas; Au = Australia; E = Europe; ME = Middle East
+; ++; +++; ++++ - increasing degree of prevalence
* these include Saint Louis encephalitis, Eastern encephalitis, Crim-Congo haemorrhagic fever, Usutu, Rocky mountain spotted fever, Sindbis, Onyongyong fever

In recent years, several other vectors have become world news: the sheep tick was discovered to be the vector of Lyme disease in 1980; the mosquito *Culex pipiens* began transmitting West Nile virus in North America in 1999; in August 2006, bluetongue virus was discovered in Belgium and the Netherlands, transmitted by biting midges and in 2007, Asian tiger mosquitoes began transmitting Chikungunya virus in northern Italy.

Other anecdotes that are worthwhile mentioning, but not very good news because of their potential impact on our society: recorded cases of canine babesiosis in the Netherlands (Nijhof et al. 2007); the establishment of the tick *Dermacentor reticulatus* in the Netherlands (de Lange et al. 2005, Nijhof et al. 2007); records of the Asian tiger mosquito in southern Germany and Switzerland; the establishment of *Aedes japonicus* in Belgium and France; annual epidemics of dengue fever in the Caribbean and South America; head lice have become highly resistant to insecticides; and London hotels are frequently infested with bedbugs (Ter Poorten and Prose 2005).

These examples demonstrate that the problems for human and animal health caused by arthropods are not uniquely linked to the least developed countries. Therefore, they need to be given highest priority by our own Ministries of Health, Welfare and Sport (VWS) as well as Agriculture, Nature and Food Quality (LNV), while at the same time we continue working with the Ministry of Development Cooperation, which has traditionally paid attention to their control.

Case study: malaria vector control

Using the example of malaria, I will explain how modern science can contribute to lasting and effective solutions for the harmful and often deadly effects caused by an insect.

The role of mosquitoes in the life cycle of malaria was discovered only as recently as 1897. Sir Ronald Ross observed the development of malaria parasites in mosquitoes, and hence established the link between parasites in the vertebrate body and the essential role of mosquitoes in their transmission from animal to animal. In 1880, Alphonse Laveran had discovered the cause of malaria when he found the *Plasmodium* parasite in the blood of French soldiers working in Algeria. Ross described an avian malaria species, but one year later the Italian scientist Grassi described the role of an anopheline mosquito in the transmission of human malaria. From then on research on malaria parasites, humans and mosquitoes has taken a huge flight until today. Both Ross and Laveran received the Nobel prize for their pioneering work on malaria.

As mosquitoes were essential to parasite transmission, the control of mosquitoes was considered the most effective and logical approach for malaria control. Early in the 20th century, scientists across the world began attacking mosquitoes. First, by draining wetlands, then by using chemical compounds that killed the mosquitoes. The Netherlands was among the forerunners in these activities, not only in the Dutch East Indies, but also in the Netherlands itself, where malaria had been highly prevalent in the coastal provinces.

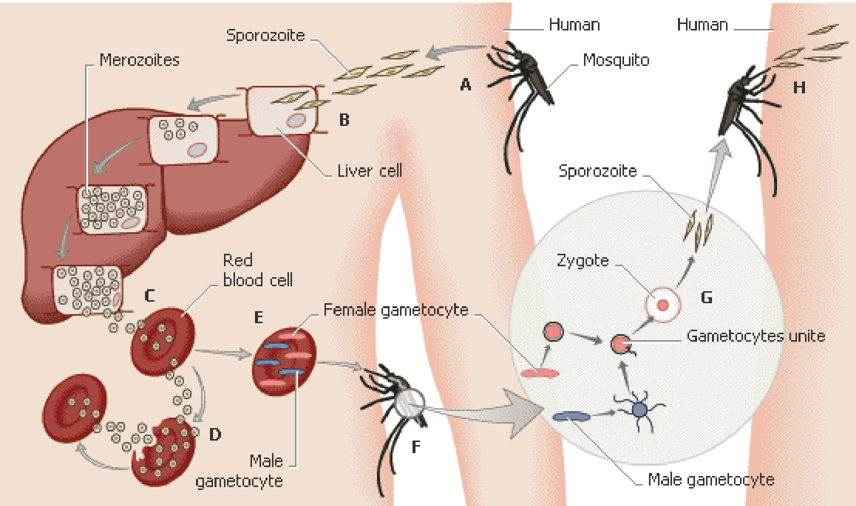

Figure 1 – The life cycle of malaria parasites (Plasmodium spp.*) (source: Encarta).*

In the Netherlands, malaria was caused by *Plasmodium vivax* and *Plasmodium malariae*, the former parasite much more important and prevalent than the latter. These parasites had developed a highly unique association with their human and mosquito hosts. In the autumn, when mosquitoes would seek shelter in stables and bedrooms, they became infected with *Plasmodium* parasites from asymptomatic malaria patients. Such mosquitoes would remain in the house or stable until the following spring. In between, some mosquitoes continued to seek a blood meal, and subsequently they could pass on the parasite to a clean host. In June, when the mosquito population had grown to sufficient size, *Plasmodium* parasites in the human host would migrate to the peripheral blood, causing high fever in parasite carriers. Thus, in the Netherlands malaria had the unusual incubation time of nine months, unlike in the tropics where it is 14 days.

In the village of Wormerveer, the village doctor Pieter C. Korteweg began reporting malaria patients in 1902, and continued doing so for many years. Because of his careful record-keeping one of the earliest and most interesting epidemiological data sets on malaria is available. Together with entomological research conducted by Nikolaas Swellengrebel, this study provides a unique insight into the behaviour of malaria in a small village in North Holland. Korteweg discovered hotspots of malaria in the village, where entire families became infected during the autumn. This was possible because large numbers of malaria mosquitoes entered the stables and bedrooms in September in search of a protected site. The mosquitoes would bite a malaria parasite carrier, develop the parasites, and then pass them on to other occupants of the same house.

It was Swellengrebel's great achievement that he practiced an early form of integrated vector control by combining larval control, drainage of surface water and adult control to the best effect. Malaria was eradicated from the Netherlands in 1959. Indeed, the Dutch example gave impulse to the malaria eradication campaign of the World Health Organization in 1955.

In that year, the World Health Assembly adopted a unanimous resolution to eradicate malaria with the aid of DDT. The insecticide DDT (Dichloro-Diphenyl-Trichloroethane)[1] was synthesized by Paul Müller in 1939. It became available at the end of World War II, when it was widely used for the

[1] 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane

control of body lice and malaria. As a result, the vector-borne disease typhus was overcome with DDT by personal treatment of lice-infested refugees and military personnel. Soon the first effective impact of DDT was seen all over the world. Müller became another Nobel prize laureate in this story.

Even by the time the WHO campaign against malaria began, however, many mosquitoes had already become resistant to DDT (Livadas and Georgopoulos 1953, Garrett-Jones and Gramiccia 1954, Chow 1958), and other, more powerful, chemicals were needed to achieve the same result. In some countries where malaria had almost been eradicated, it returned with a vengeance. In other, poorer, regions of the world, malaria was not effectively controlled, and in fact expanded and increased in incidence. By 1969 the WHO strategy of malaria eradication was abandoned for logistical reasons and the presumed wide-scale resistance to the insecticide DDT.

In 1962 Rachel Carson published her world-famous book "Silent Spring", in which she described a lake in North America, where loons no longer sang and fish and other wildlife were disappearing fast, or had become sterile. Her book heralded the dawn of the environmental movement and environmental conscience. The effects of DDT and its sibling compounds such as dieldrin, aldrin and endrin became noticeable everywhere, and people realized that some of these products had an almost eternal half-life. The breakdown product of DDT, DDE, evaporated in the atmosphere, to be deposited around the polar circles, where these compounds had never been used, threatening the health of people and wildlife there (Karlaganis et al. 2001). DDT and its derivatives were banned in many countries in the 1970's, primarily because of their environmental impact and potential negative effects on human health. As these products continued to be used in the least developed countries, mostly in agriculture, the United Nations took the initiative to ban 12 of the most persistent of this group of compounds, the "dirty dozen". In 2004, the Stockholm Convention on persistent organic pollutants came into effect, commonly named the POPs convention. Under this treaty, the production and/or use of 12 organic compounds, among which nine pesticides, PCBs and dioxins and furans, will be phased out. In the absence of effective alternative solutions, however, exemptions are granted for a few important and persistent pests: termites, some ectoparasites, and disease vectors. The latter concerns mostly the use of DDT for malaria control. DDT may only be used on condition that research into effective alternative strategies for malaria mosquito control continues.

The Stockholm Convention has had an extraordinary, and in my view undesirable, side effect: countries that had not used DDT for more than 30 years were now eager to apply it again for malaria control. This happened alongside the rapid expansion of the use of insecticide-treated bednets. It is alarming to note that DDT has suddenly become popular again (Weissmann 2006, Sadasivaiah et al. 2007).

In the long period between 1969 and 1999, malaria control had come almost to a standstill and became dependent on drug treatment as the main strategy. So much so, that with the rapidly growing population of the least developed countries, the disease was claiming more lives than ever, and affecting half a billion people each year. *Plasmodium* parasites developed drug resistance and only few effective anti-mosquito products were available, at high costs. On the African continent, South Africa was the only country that successfully combated the disease, whilst elsewhere on the continent the disease expanded.

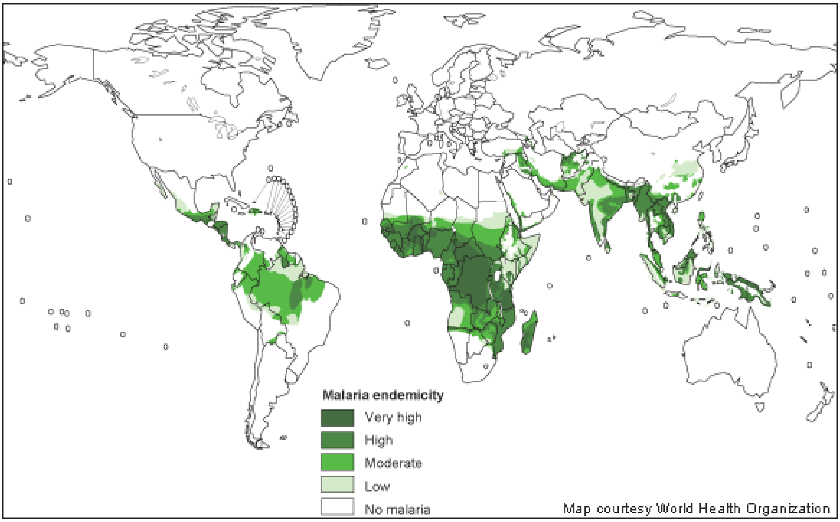

Figure 2 – World distribution of malaria in 2008 (source: World Health Organization).

Today, malaria is found in a large part of the world, exposing 4 billion people to risk, and annually infecting 500-600 million people (Snow et al. 2005). Existing control strategies, based on drug treatment, are not sufficiently effective. For this reason, certain countries in Africa are again looking at DDT to solve their malaria problems.

In the light of this serious malaria situation, one wonders whether novel strategies are being developed that could provide a lasting solution to the malaria problem. Is there reason for hope? and if so, which strategy is available or should be developed?

On the medical side, the combination drug ACT (artemisinine combination treatment) was introduced in recent years, providing a remarkably effective treatment for malaria. Indeed, when ACT is well administered, many lives can be saved. The remarkable character of this drug is that it is of botanic origin, having been used as tea in China for thousands of years. As a treatment for malaria it has less severe side effects than quinine, the world's oldest botanical used for malaria control.

At the same time as the introduction of ACT, bednets impregnated with insecticides were developed. These nets provide protection from mosquitoes, and the insecticide impregnated in the netting is slowly released into the environment so that mosquitoes are repelled by it, and will not touch the net. The advantage of the insecticide treatment is that nets, even when they get torn, will still provide protection because of the repellent effect of the insecticide. The combined strategy of combination drug treatment and impregnated bednet use has even given rise to expectations of malaria control within the near future (Aguas et al. 2008). This development has encouraged the Bill and Melinda Gates Foundation in October 2007 to launch a new initiative to eradicate malaria.

Whereas the use of insecticide-treated nets may look like a splendid solution for the malaria problem (Lengeler 2004), I would like to raise an objection to this unidirectional approach and propose several, equally promising, alternatives.

The widespread use of insecticide-treated bednets and the re-introduction of DDT for malaria control poses a problem: Bednets are impregnated with pyrethroids, which express cross-resistance with DDT and other organochlorines. Thus, the simultaneous use of pyrethroids and organochlorines enhances the spread of insecticide resistance. Whereas the pyrethroids are stably impregnated in the bednet fabric, the DDT arrives in drums and could potentially be used for the control of pests in agriculture. In fact, this is what frequently happens. Furthermore, the wide scale use of pyrethroids in agriculture has caused insecticide resistance in malaria mosquitoes: the larval stages of the mosquitoes develop in water that contains run-off insecticides from the crops. This has led to a considerable degree of insecticide resistance in West and southern Africa (N'Guessan et al. 2007). In a recent study in southern Mexico, it was found that malaria mosquitoes developed resistance to a mosaic of insecticides within 3 years after introduction of these compounds (Penilla et al. 2007). How much more evidence is needed before scientists and regulatory authorities realize that the use of insecticides is an unsustainable approach? The target insects will inevitably develop resistance. At present more than 120 malaria mosquito species have developed resistance to a wide variety of insecticides, and the current widespread use of bednets and the re-introduction of indoor residual spraying is likely to enhance this further (Coetzee et al. 1999, Hemingway and Ranson 2000, Hemingway et al. 2002, Nauen 2007).

Figure 3 – A bed net, treated with the insecticide permethrin, protects people significantly from malaria infections (source: World Health Organization).

In addition, the use of DDT has a proven history of accumulation in tissues of higher vertebrates, where it causes significant effects on reproductive health and can impair the functioning of the nervous system (van Wendel de Joode et al. 2001, Rogan and Chen 2005, Seagren 2005, Aneck-Hahn et al. 2007, Torres-Sanchez et al. 2007). This was of course one of the reasons to phase out the production and continued use of DDT, along with other persistent organic pollutants.

If not insecticides, what are the alternatives for malaria control? And how difficult would it be to overcome the public belief that insecticide-treated bednets are the best solution for malaria control? Consider the example of my mentor, professor Joop van Lenteren: in the 1970's he pioneered biological control of greenhouse pests in the Netherlands, convinced that pesticides would only lead to problems. Fighting against the strong force of the pesticide industry as well as the scientific world, he continued with his experiments. Today, he is recognized as the father of biological control in greenhouses, and >95% of all greenhouse vegetables in western Europe are currently produced under biological control, grown without insecticides (Lewis et al. 1997, van Lenteren et al. 2006, Bale et al. 2008). Van Lenteren received the prestigious Royal Dutch Shell prize for sustainable development and energy because of his groundbreaking work on pest control. If this can be done for a horticultural pest, why don't we do this for a disease vector as well? It is my goal to be able to control malaria without chemical pesticides.

All malaria control strategies directed at the mosquito vector are based on the simple principle that a reduction in biting will lead to reduced parasite transmission. This principle has been mathematically termed the entomological inoculation rate (EIR), which is the product of the fraction of the mosquito population biting humans and the proportion infected with malaria parasites. There is a direct relationship between malaria and the EIR, there being morbidity when the EIR is high as well (Smith et al. 2006). By removal of the vector with whatever strategy, the EIR will be reduced and consequently malaria disease will decrease as well. Conventional insecticides meet the requirement of effectively removing disease vectors, and hence, their use will lower the entomological inoculation rate. For reasons discussed above, they should, however, be replaced by other agents.

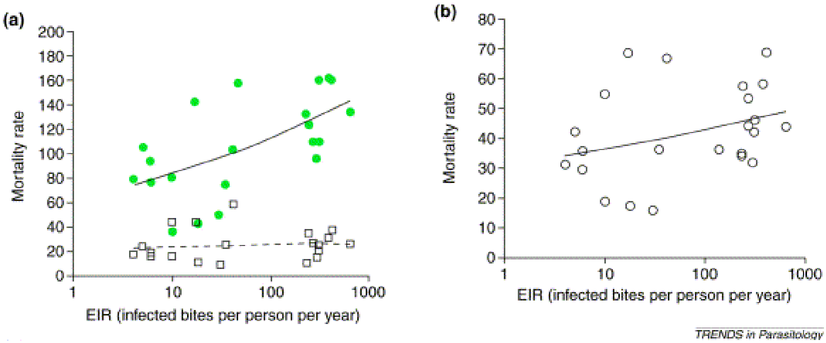

Figure 4 – (a) African child mortality rates by entomological inoculation rate (EIR) for Plasmodium falciparum. *Age specific rates. (b) Infant mortality rate (0–11 months of age), closed circles; child mortality rate (12–59 months of age), open squares. Overall (0–59 months of age), open circles. (source: Smith, T.A., Leuenberger, R. & Lengeler, C. (2001) Trends in Parasitology 17: 145-149).*

In the last decade, major advances have been made with novel tools for malaria vector control. These vary from improvement of houses (Lindsay et al. 2003), environmental management (Keiser et al. 2005), biological control of larvae (Walker and Lynch 2007), adult mosquito control with entomopathogenic fungi (Scholte et al. 2005), behavioural interventions with odour-baited traps (Takken and Knols 1999), and the development of genetically-modified mosquitoes that carry genetic traits making them non-susceptible to malaria parasites (Catteruccia 2007). I will briefly review these techniques (Table 2).

House improvement - Many malaria mosquitoes inherently attack their blood hosts only at night, when people are indoors and asleep. Hence, a physical barrier preventing a mosquito from entering a house will contribute to less biting, and less malaria. Poverty, however, forces people to live in poor houses without mosquito screening and therefore is a major factor in the continued high exposure to mosquito bites. The improvement of houses, by better house design and screening will directly contribute to less malaria (Lindsay et al. 2002).

Table 2 – Novel tools for malaria vector control

Tool	Mosquito life stage under attack	Remarks
House improvement	Adults	Screening, Brick building
Environmental management	Larvae	Can be combined with innovative agricultural methods
Biological control	Aquatic stage (larvae)	Legislation needed for release of biologicals
	Terrestrial stage (adults)	Legislation needed for release of biologicals
Biorational control	Larvae	Insect growth regulator
Behavioural manipulation	Adults	Feasible at household and village scale
Genetic control	All life stages	Expensive in development stage; requires legislation for release of GMO and/or sterile insects

Environmental (water) management - The nurseries of mosquitoes are pools, puddles and other collections of water in which larvae can develop. Malaria was eradicated from much of Italy, the continental USA and China by drainage of these bodies of water. Where possible, this is the simplest tool available for effective mosquito control, and farming communities can be encouraged to design water systems that reduce the probability of mosquito development. This is often not considered high technology, and therefore water management for public health does not receive much priority at the level of policy makers. Yet, it is probably the most effective and attractive tool of malaria control (Keiser et al. 2005)

Biological control of larvae - In recent years, several exciting and highly effective biological control agents have become available, having great impact on the survival of malaria mosquito larvae. One of these, *Bacillus thuringiensis israeliensis*, was shown to be effective against a wide range of malaria mosquitoes (Fillinger and Lindsay 2006). Unlike with conventional insecticides, resistance to Bti is unlikely to develop because of its unique strategy of expressing several toxins at the same time (Federici 2005). Other agents for killing mosquito larvae include botanical products, predatory fish, fungi and nematods. Compounds that cover the water layer so that mosquito larvae are asphyxiated, also show great promise, provided they are cheap, non-polluting and preferably exhibit a long residual life.

Biological control of adults - In 2005 the Laboratory of Entomology caught the world's attention by publishing the novel use of an entomopathogenic fungus for the control of adult malaria mosquitoes. It was shown that the fungus *Metarhizium anisopliae* killed adult mosquitoes that had become infected in deliberately-treated houses in an African village. Here, for the first time, an alternative for chemical insecticides had been found (Scholte et al. 2005). The fungus has several advantages over insecticides: it is a natural product, it can be mass-produced without difficulty, and because of its biological properties, development of resistance is unlikely (Thomas and Read 2007). Exciting additional advantage is that fungus-infected mosquitoes are no longer able to develop malaria parasites (Blanford et al. 2005).Work is in progress to develop this novel tool into a strategic instrument for malaria control.

Behavioural manipulation - Mosquitoes locate their human and animal hosts by their odours. African malaria mosquitoes are remarkable in that they prefer to feed on human hosts, which enhances the mosquito-host contact and therefore favours the transmission of malaria parasites (Takken and Knols 1999). The odours that affect this behaviour are mainly derived from the human skin, and recent work in Wageningen has led to the development of an attractive blend with which malaria mosquitoes can be successfully caught in an African field situation. Thus, one can envisage that the behaviour of mosquitoes can be manipulated by strategic application of odorant targets in and around houses, leading to reduced biting. In combination with an effective killing agent, such as the entomopathogenic fungus, odour-baited traps may become an excellent tool in the control of malaria mosquitoes. Other behavioural strategies that can be influenced with odorants are mating behaviour and oviposition behaviour. Here in Wageningen we have the unique ability to study these behaviours using sophisticated chemical technology, electrophysiology and behavioural ecology. This type of research is also conducted by others at the Laboratory of Entomology where it benefits from complementary research on different insect systems (Dicke 2000).

Genetic control - Recombinant DNA technology, jointly with molecular genetics, has allowed the development of tools that can modify the genetic structure of organisms, including disease vectors. The genes that regulate the establishment and development of *Plasmodium* parasites in mosquitoes, for example, can be manipulated by silencing with RNAi technology or by knock-out systems. Sequencing of the genetic composition of *Plasmodium* and the malaria vector *Anopheles gambiae* have allowed for a rapid identification of genes that are upregulated in parasite-mosquito interaction. Several mosquito lines are now in laboratory cultures that could potentially be used for genetic manipulation of malaria mosquito populations. Whilst this technology is extremely useful in the unravelling of fundamental mechanisms of parasite-vector interactions, such as the passage of parasites through the midgut, or the evasion of insect immune systems, we should question the ethics of its use in the field. In theory, a genetically-modified mosquito that is incapable of transmitting malaria seems the ideal solution to this ancient disease. In practice, a multitude of problems needs to be overcome before this technology can become reality (Scott et al. 2002, Benedict et al. 2008).

Summarizing the future of malaria vector control: it is clear that the large-scale use of conventional insecticides has had its longest time and is not sustainable. Effective tools, with no or significantly less risk attached, are waiting in the wings and efforts should be undertaken to bring them to the forefront, so that public health officials and policy makers will give them the place in disease control they deserve. The catch phrase is "integrated vector management", which allows for the combination of tools that promise the greatest effect with a low environmental impact. Because we have not yet had much experience with integrated vector management, I dare scientists to take up the challenge and make it work. Only then can we convince the disease-control strategists that IVM is the way forward. Malaria control, therefore, has arrived at a new age, and will witness the introduction of methods not seen before. These tools are needed, more so than ever, to make a lasting and effective input in the reduction of malaria, or even to assist with malaria eradication in selected geographic regions.

What can we learn from the example of malaria and malaria vectors? Vectors have their domicile in complex environments, and appear highly adaptable to such environments. When they have formed an association with a pathogenic agent, this will often accompany the vector to a new environment, such as urban areas (e.g., malaria, dengue) or beyond classical distribution limits of parasites and/or vectors (e.g., *Aedes albopictus* and Chikungunya virus; *Culicoides* and bluetongue virus).

Prospects for innovative arthropod-borne disease control

Let me return now to the broader topic of insects and disease. Fifty years ago, most insects affecting human and animal health were attacked or kept under control with insecticides. As with malaria mosquitoes, however, many of these pests developed insecticide resistance, demonstrating that this chemical strategy was limited and could only last for a short period of time. Moreover, unlike in agriculture, public health pesticides needed to be safe for use on and around humans. Few compounds, however, met this condition and had to be phased out or abandoned for safety reasons. This has sometimes placed vector control in a crisis, for lack of an effective alternative.

In much of the temperate climatic regions, health problems caused by insects, ticks and other arthropods were thought solved in the latter half of the 20th century. For example, by 1980, head lice were considered a problem of the past, bedbugs were no longer seen, and malaria was eradicated from Europe and the continental USA. In the South American jungle, the yellow fever mosquito, *Aedes aegypti*, was suppressed and eventually eradicated. In the livestock industry, the American cattle tick *Rhipicephalus microplus* (formerly *Boophilus microplus*) was eradicated from the southern United States, and in Australia this tick species is controlled by immunization of cattle with tick antigens (Graham and Hourrigan 1977, Willadsen et al. 1995). Huge successes were achieved with the sterile insect technique for the control of the cattle screwworm fly *Cochlyomia hominivorax* and the United States and Mexico as well as much of Central America are now free of this harmful pest (Wyss 2000).

Table 3 – Recent introductions and/or resurgences of vector-borne pathogens and arthropod pests of public and animal health significance

	Origin	Areas of invasion or resurgence	Invasion or resurgence
Pathogen			
Dengue	Southeast Asia	Africa, Americas	Invasion
West Nile virus	Africa	Americas	Invasion
Chikungunya	Africa	Italy	Invasion
Bluetongue virus	Africa	Europe	Invasion
African horse sickness	Africa	Iberian peninsula	Invasion
Usutu virus	Africa	Europe, Australia	Invasion
Arthropod species			
Aedes albopictus (Asian tiger mosquito)	Southeast Asia	Americas, Africa, southern Europe	Invasion
Aedes japonicus	East Asia	USA, France	Invasion
Dermacentor reticulatus	Southern Europe	The Netherlands	Invasion
Bedbug		Worldwide	Resurgence
Head louse		Industrialized countries	Resurgence

Today it has become apparent that many of these successes have turned out to be temporary, as many countries are facing resurgence or invasions of pest insects and/or the diseases carried by them (Table 3). Increased traffic, trade and human movement has contributed to this situation, but factors such as environmental change, climate change and agricultural use of pesticides are additional factors leading to the current state of affairs. Consider climate change: insects and ticks are cold-blooded animals, and depend on the ambient temperatures for their growth and development. Typically, at higher temperatures the life cycle is shortened, and generations can succeed each other rapidly. The parasites and pathogens that are transmitted by these arthropods also thrive at higher temperatures. Thus, it is expected that climate change will favour disease vectors. We must, therefore, be prepared that a range of insects and/or the pathogens they can transmit, might shift to higher latitudes (Epstein 2005, Patz and Olson 2006).

Our lifestyle, however, has also contributed to these events: by intensifying trade and commerce, as well as by frequent travel, many diseases are being introduced into new environments where they can adapt to local vectors (Mehlhorn et al. 2007, Takken et al. 2007). The arrival of bluetongue in north-western Europe in 2006 is a clear example where trade and climate conspired to introduce an arbovirus to a new geographic region. A similar event affected the United States in 1999, when the West Nile virus was introduced, presumably with an infected bird from Israel (Deubel et al. 2001). Management strategies of forest areas can also contribute to vector-borne disease, as appears to be the case for Lyme disease. In the Netherlands a large increase in prevalence of Lyme disease has occurred between 1994 and 2005, presumably as a result of ecological measures that supported forest expansion and wildlife reserves (Hofhuis et al. 2006, Prins 2007). In addition, the ticks that are responsible for the transmission of Lyme disease remain active for longer time periods under increasing temperatures (Randolph 2004). In South America, the unrestricted slashing of rainforest has led to unprecedented increases in malaria incidence (de Castro et al. 2006, Singer and De Castro 2006).

Future threats caused by arthropod vectors include dengue, bluetongue, leishmaniasis, tick-borne infections and novel arbo-viral diseases. Several of these diseases may affect both humans and animals, and are therefore of great significance for our society. In addition, it is likely that environmental changes such as climate change will cause a shift in distribution of insects and ticks into areas where they until now have posed few problems. A new phenomenon has been added to this spectrum: the creation of new forest systems by withdrawing agricultural fields from agricultural production (Prins 2007).

Should we allow the emergence and invasion of pests and diseases to happen, or should we fight them? We do not want people to die or suffer because of the emergence of a new health risk. Thus, measures must be taken to prevent the outbreak of new vector-borne diseases. With few exceptions, insect pests and vectors need to be addressed with direct impact, rather than waiting for a vaccine or safe drug. The currently-available research tools promise much for the development of more effective methods that can suppress, or even eradicate, human and animal disease caused by insects.

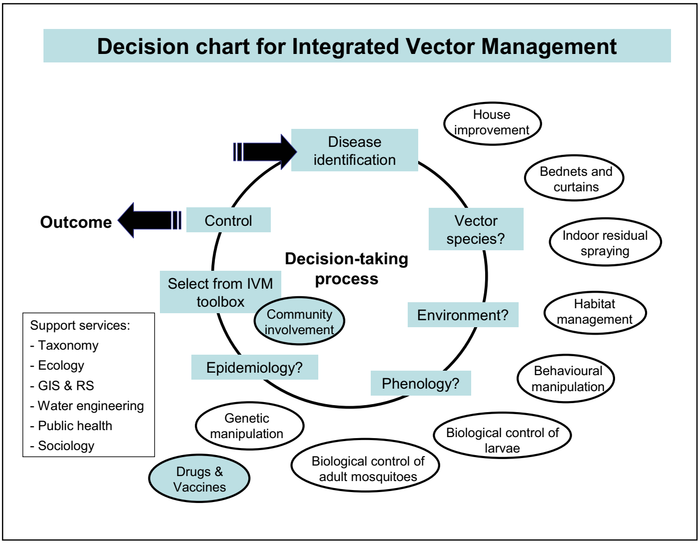

Figure 5 – Decision chart for integrated vector management, from problem identification to outcome.

Some recent advances in science and technology that are essential for a rapid understanding of problems caused by disease vectors and other human and animal arthropod pests include the extraordinary developments in the world of molecular genetics, allowing us to provide insects with a bar-code for rapid and accurate species determination, even to subspecies level (Miller 2007) as well as to sequence the entire genetic structure of the insect, so that biological and ecological processes in vectors and their environment can be better understood (Holt and et al. 2002, Waterhouse et al. 2008). Another discipline that has made great progress for a better understanding of vector-host and vector-pathogen interactions is that of chemical ecology. Here, volatiles are examined that manipulate the behaviour of the target insects and ticks and can profoundly affect our understanding of the biology of these organisms (Harborne 1999, Birkett et al. 2004). Third, new developments in geographic information systems and remote sensing have opened up our understanding of disease epidemiology in relation to environmental factors such as climate, demography, topography and land cover. For the first time, habitats can be effectively identified using remote sensing and linked to each other (Ostfeld et al. 2005).This helps to make vector control more effective and efficient. All these technologies, molecular biology, chemical ecology and GIS and RS sciences, have been incorporated in vector ecology and will be essential in the development of novel intervention strategies for disease control.

As many of these disciplines are already present in Wageningen, I propose the development of a Wageningen strategy for the management of arthropods affecting human and animal health. This approach would fit with the current mission of Wageningen University and Research Centre, which focuses on health, lifestyle and livelihood; food and food production; and the living environment.

Mr. Rector, I have outlined how Wageningen University and Research Centre can play a vital and constructive role in the future of public and animal health. I am convinced that with a collaborative approach we can continue and possibly expand our activities in these fields, specifically by enhancing our national and international cooperation. Undergraduate and graduate students should participate in these programmes, so that they get hands-on experience in these important research programmes, providing them with an opportunity to work on their own future, while participating in the development of a healthier and safer planet. Many of our study programmes also touch on these topics. Hence, education and research provide unique opportunities for the development of sustainable tools for health control.

Insects and disease have shaped our society as we know it, and are likely to do so for the foreseeable future. Current scientific progress, aided by information and communication technology, however, provide opportunities for combating vector-borne disease as never before, and I feel privileged to be part of an academic community that is at the forefront of these activities.

Acknowledgements

At the conclusion of this speech, I wish to express my gratitude to a number of individuals who have been instrumental in the research and education described above.
Joop van Lenteren: the occasion of our first meeting was unusual, the reason being a near fatal accident with an aircraft in Africa. I am deeply grateful for the support and encouragement you have provided from my fledgling start at the Laboratory of Entomology.
Arnold van Huis: together we have kept the Wageningen expertise in tropical entomology alive, realizing that multiple, shared, research is needed before development can be achieved and implemented to where it stands today. Thank you for supporting me and working with me on this endeavour.
Marcel Dicke: you are not only my current boss, but also a strong supporter and friend. I value the space you have provided to develop our programme on the ecology of disease vectors, and the high degree of independence that is necessary to develop new programmes and projects. The current chair in Medical and Veterinary Entomology would not have been created without your wisdom and support.
Bart Knols: your eagerness and curiosity as a student and young scientist have certainly kept me busy, but also stimulated me to seek collaboration with colleagues in the country and abroad. I look forward to a continuation of our joint work.
The students and colleagues at the Laboratory of Entomology: I value your almost-unlimited enthusiasm for our joint research, which can be demanding because it is often highly unusual. I look forward to the continuation of working with you.
Dearest Françoise, you have followed my career path through many countries and jobs, until we landed in Wageningen. I deeply appreciate the time you have taken to look after our family, especially during the many weeks I was away on duty travel. You have allowed me to arrive where I am now, and I hope that jointly we can enjoy the coming years by balancing exciting science with private activities.
Nicolas and Daniel, you both have probably suffered most from my frequent

absences from Wageningen. I have therefore missed some critical moments in your various life stages, but am proud to see where you have both arrived at! Thank you for your continued interest in my travels and work. I will continue to share this with you.

I thank the Academic Board of Wageningen University for having the confidence to appoint me in the position of Professor of Medical and Veterinary Entomology. I intend to practice this field of science in a manner worthy of its significance and explore possibilities for embedding this field permanently in Wageningen.

Mr. Rector, ladies and gentlemen, I thank you for your attention.

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