1. Strategic use of chemical ecology for vector-borne disease control

Willem Takken and Bart G.J. Knols

Abstract

In the epidemiology and control of vector-borne diseases an accurate estimate of parasite and pathogen transmission is required. This can be achieved by monitoring the vector population using traps provided with attractive cues. Volatile chemicals are the principle cues with which the disease vectors locate their vertebrate hosts. Natural and synthetic blends of such chemicals can be used to manipulate the vectors, so that transmission risk can be determined and, in some cases, the vector population can be killed. Novel scientific developments, including molecular genetics, analytic chemistry and odour-release technologies provide opportunities for the effective use of chemical ecology in vector-borne disease control.

Keywords: olfaction, insects, ticks, behaviour, disease transmission, nuisance, attractant, repellent

Introduction

In the last decade nuisance insects and disease vectors have received increasing attention because of their continuing and devastating effects on human and animal health. Examples are recent outbreaks of chikungunya fever in the Indian Ocean, SE India and Italy (Erin Staples *et al.* 2009), the large number of recorded dengue outbreaks in South America (Barclay 2008) and the arrival of bluetongue virus in NW Europe (Carpenter *et al.* 2009). In addition, the rapid growth of the world population coupled with increasing poverty in resource-poor countries is the cause of much suffering from neglected vector-borne diseases such as malaria, leishmaniasis and trypanosomiasis (Mathers *et al.* 2007). Lastly, the current debate on climate change and its potential effects on human health is causing global concern about emerging diseases such as West Nile virus, Lyme disease and other tick-borne diseases (Epstein 2001, Gould and Higgs 2009, Jones *et al.* 2008). Whereas for several of these diseases effective intervention strategies are available, and hence their control can be implemented, for many of them the current control strategy is inadequate. With some exceptions, effective vaccines are lacking, parasites have developed resistance against drugs, and vector control efforts are hampered by insecticide resistance, technologically inadequate tools and lack of resources.

It is widely agreed that the first step in monitoring vector-borne disease is accurate risk assessment (Hay *et al.* 2004, Mathers *et al.* 2007). This information is needed to study the epidemiology of the disease, and to predict its course in time and space. The basic reproductive number (R_0) (Hartemink *et al.* 2008, Smith *et al.* 2007) is used to express disease risk, and as the biting rate of disease vectors is one of the critical parameters in R_0, tools to accurately measure this are essential. Examples in which these data are being widely used are malaria and dengue control programmes: in endemic situations vector densities provide knowledge on spatial and temporal distribution of biting intensities, while in epidemic situations, vector populations are measured so that the course of the outbreak can be monitored. Also, the outcome of vector-targeted interventions, aimed at the interruption of parasite/pathogen transmission, can be assessed when accurate data on vector densities are available. Vectors are also collected to determine their infections with disease agents: the intensity of disease transmission the product of vector density and parasite/pathogen infection rate. In spite of the importance of accurate sampling of disease vectors, the methodologies used for insect collection are in many cases based on perception rather than on accurate knowledge of vector behaviour. This is because information on vector-host interactions (at which level the parasites/pathogens are being transferred) is in many cases poor or lacking. It is therefore of relevance that this knowledge be expanded in order to obtain better, more precise, data on vector biting density and intensity of parasite transmission.

Since the discovery of the role of arthropods in disease transmission, entomologists have worked on the development of tools for vector surveillance, and a wide range of traps is available with which the vector population can be monitored (Qiu *et al.* 2007, Service 1993). Traps are designed to attract the target insect(s) using sensory cues such as sound, colour and odour. As chemical signals are the principal cues with which arthropods identify their blood hosts, many traps employ odorants to lure the vectors to the trap. The odorants used vary from natural host odours, synthetic blends of compounds mimicking host odours, or non-host related chemical compounds that have been found to be attractive to the vectors. Harris (1938) and Van Thiel (1935) were among the first to report on the use of host odours to trap tsetse flies and mosquitoes, respectively. It was also established that carbon dioxide (CO_2) acts as a universal attractant for many blood-feeding insects, and many traps are baited with this compound. For example, the Centre for Disease Control miniature light trap (CDC light trap) (Sudia and Chamberlain 1962) was reported to produce significantly-enhanced catches of mosquitoes when baited with dry ice (Newhouse *et al.* 1966). The CO_2-baited CDC trap was the gold standard for establishing mosquito densities for many years. In the tropics, CO_2 was replaced by natural human emanations by operating the CDC trap next to a bed net under which a human spent the night (Garrett-Jones and Magayuka 1975). Although these odour-baited traps collected disease vectors, the trap collections represented only crude data on vector densities, and more accurate measurements were needed.

In the 1970s, Vale (1974), dissatisfied with the variable results of odour-baited traps, began to experiment with natural host odours to investigate the behaviour of tsetse flies in Zimbabwe. By using an elegant design of electrified grids and artificial host models, Vale demonstrated that natural host odours were the principle cues that led tsetse flies to the vicinity of their blood hosts (Vale 1993). The studies on tsetse olfactory behaviour are still considered to be classic methods for investigating insect behaviour with respect to their vertebrate hosts. Gillies and Wilkes (1968) demonstrated that mosquitoes could also be manipulated with host odours, and it was soon found that synthetic blends of odorants could be used to manipulate mosquito populations (Takken and Kline 1989). These behavioural studies were gradually augmented with physiological studies to reveal the sensory processes that made the insects respond to the odorants (Cork 1996, Davis and Sokolove 1976). The advent of molecular genetics has allowed for detailed insight in the genetics and molecular regulation of insect olfaction, which provides fundamental knowledge on the regulation of insect behaviour (Jacquin Joly and Merlin 2004, Lessing and Carlson 1999, Touhara and Vosshall 2009). This, in turn is being used for the identification of chemical compounds that affect vector-host interactions, so that the target vectors can be more effectively lured to sampling devices and/or removed from the environment as a tool for disease control.

In future, odorants will increasingly be used for the monitoring of vector-borne disease transmission risk as well as for vector control. It is therefore appropriate that the current volume of the Ecology and Control of Vector-borne Diseases has brought together reviews of the state-of-the-art of this topic, from the molecular regulation of olfactory senses (Chapter 2) to field applications of odorants for disease control (Chapter 17). As many disease vectors belong to the insect order of Diptera, this group of insects is discussed in detail, with mosquitoes being the example for detailed explanation of olfactory regulation. Chapters on blood-feeding bugs, vectors of Chagas disease, and blood-feeding ticks, vectors of a variety of parasites and pathogens, are included as well. Finally, as it is increasingly becoming apparent that the olfactory behaviour of insects and ticks is often mediated by parasites, a chapter on the latest knowledge of this field of science is also included. Odorants are not only used to attract insects and ticks, but they can also be used to protect blood hosts from being attacked (Katz *et al.* 2008). In many cases odorants act as deterrents or repellents, and where applicable, this aspect of olfaction is discussed as well.

The ecology of vector-borne diseases is much determined by the association between vectors, parasites and hosts, which is in turn strongly mediated by chemical cues. The chapters in this volume demonstrate that detailed studies on insect olfaction contribute to our understanding of the individual components regulating this process, and contribute to finding effective solutions for disease control.

References

Barclay E (2008) Is climate change affecting dengue in the Americas? The Lancet 371: 973-974.

Carpenter S, Wilson A and Mellor PS (2009) *Culicoides* and the emergence of bluetongue virus in northern Europe. Trends Microb 17: 172-178.

Cork A (1996) Olfactory basis of host location by mosquitoes and other haematophagous Diptera. In: Bock GR and Cardew G (eds) Olfaction in mosquito host interactions. CIBA Foundation Symposium 200. Wiley, Chichester, UK, pp 71-88.

Davis EE and Sokolove PG (1976) Lactic acid-sensitive receptors on the antennae of the mosquito, *Aedes aegypti*. J Comp Physiol 105: 43-54.

Epstein PR (2001) Climate change and emerging infectious diseases: review. Microbes and Infection 3: 747-754.

Erin Staples J, Breiman RF and Powers AM (2009) Chikungunya fever: an epidemiological review of a re-emerging infectious disease. Clinical Inf Dis 49: 942-948.

Garrett-Jones C and Magayuka SA (1975) Studies on the natural incidence of *Plasmodium* and *Wuchereria* infections on *Anopheles* in rural East Africa: I-assessment of densities by trapping hungry female *Anopheles gambiae* Giles, Species A. WHO/VBC 75.145 Geneva Switzerland.

Gillies MT and Wilkes TJ (1968) A comparison of the range of attraction of animal baits and of carbon dioxide for some West African mosquitoes. Bull Entomol Res 59: 441-456.

Gould EA and Higgs S (2009) Impact of climate change and other factors on emerging arbovirus diseases. Trans Royal Soc Trop Med and Hygiene 103: 109-121.

Harris RHTP (1938) The control and possible extermination of the tsetse by trapping. Acta Conventus Tertii de Tropicis Atque Malariae Morbis 1: 663-677.

Hartemink NA, Randolph SE, Davis SA and Heesterbeek JA (2008) The basic reproduction number for complex disease systems: defining R(0) for tick-borne infections. American Naturalist 171: 743-754.

Hay SI, Guerra CA, Tatem AJ, Noor AM and Snow RW (2004) The global distribution and population at risk of malaria: past, present, and future. Lancet Infectious Diseases 4: 327-336.

Jacquin Joly E and Merlin C (2004) Insect olfactory receptors: contributions of molecular biology to chemical ecology. J Chem Ecology 30: 2359-2397.

Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL and Daszak P (2008) Global trends in emerging infectious diseases. Nature 451: 990-993.

Katz TM, Miller JH and Hebert AA (2008) Insect repellents: historical perspectives and new developments. J Am Acad Derm 58: 865-871.

Lessing D and Carlson JR (1999) Chemosensory behaviour: the path from stimulus to response. Curr Opinion Neurobiol 9: 766-771.

Mathers CD, Ezzati M and Lopez AD (2007) Measuring the burden of neglected tropical diseases: the global burden of disease framework. PLoS Negl Trop Dis 1: e114.

Newhouse VF, Chamberlain RW, Johnston JG and Sudia WD (1966) Use of dry ice to increase mosquito catches of the CDC miniature light trap. Mosquito News 26: 30-35.

Qiu YT, Spitzen J, Smallegange RC and Knols BGJ (2007) Monitoring systems for adult insect pests and disease vectors. In: Takken W and Knols BGJ (eds) Ecology and control of vector-borne diseases, Vol. 1: emerging pests and vector-borne diseases in Europe. Wageningen Academic Publishers, Wageningen, the Netherlands, pp 329-353.

Service MW (1993) Mosquito ecology - field sampling methods. second edn. Elsevier Applied Science, London, UK.

Smith DL, McKenzie FE, Snow RW and Hay SI (2007) Revisiting the basic reproductive number for malaria and its implications for malaria control. Plos Biology 5: e42.

Sudia WD and Chamberlain RW (1962) Battery-operated light trap, an improved model. Mosquito News 22: 126-129.

Takken W and Kline DL (1989) Carbon dioxide and 1-octen-3-ol as mosquito attractants. J Am Mosquito Control Ass 5: 311-316.

Touhara K and Vosshall LB (2009) Sensing odorants and pheromones with chemosensory receptors. Annual Rev Physiol 71: 307-332.

Vale GA (1974) New field methods for studying the responses of tsetse flies (Diptera, Glossinidae) to hosts. Bull Ent Res 64: 199-208.

Vale GA (1993) Development of baits for Tsetse flies (Diptera: Glossinidae) in Zimbabwe. J Med Ent 30: 831-842.

Van Thiel PH (1935) Onderzoekingen omtrent den gedrag van *Anopheles* ten opzichte van mensch en dier, mede in verband met rassenstudie bij *Anopheles maculipennis* (Studies on the behaviour of *Anopheles* around humans and animals, associated with a species-specific study of *Anopheles maculipennis*). Gen Tijdschr Ned Indië 75: 2101-2181.