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Application of genetically modified mosquitoes in national vector control programmes: thoughts on integrated control

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Abstract

Advances in transgenic technology have allowed the development of genetically transformed insects that have reduced ability to support the development of disease pathogens. The integration of this new method within national vector control programmes is indeed the biggest challenge, notwithstanding the current weak health systems in most disease-endemic countries (DECs) to efficiently apply vector control interventions. Moreover, where integration is considered, it is essential that reliable data are available on the multiple effects of the interventions. This should be done in parallel to the general strengthening of both human, technical, financial and physical resources at all levels of the national health system.
Keywords: genetically modified mosquitoes; integrated vector management; transgenesis; vector control programmes

Introduction

The long-term goal of research on genetically modified mosquitoes is to develop strains that are unable to support the development of human pathogens and then introduce and drive such a trait into natural insect vector populations. Progress has been achieved in two important disease vectors – *Anopheles stephensi* (vector species of malaria in South Asia) and *Aedes aegypti* (vector of dengue and yellow fever) (Moreira et al. 2002). In *An. gambiae*, on the other hand, germline transformation has been accomplished but not yet with any potential useful effects.

Knowledge from the work on *An. stephensi* and *Ae. aegypti* has allowed the construction of refractory mosquitoes with the potential to be extended to other vector species and to other important biological and behavioural traits that are relevant in vector disease transmission. For example, the development of a ‘genetically transformed’ mosquito that no longer has a preference for human blood would be a breakthrough (Coluzzi and Costantini 2002). The biggest challenge, however, is how and when such a tool can be integrated into existing national vector control programmes.

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A global trend – from disease-specific to integrated control

From a programmatic point of view, the current global trend is to move away from vertical or disease-specific programmes. One such approach in vector-borne disease control is Integrated Vector Management (IVM). This is an approach that emphasizes the promotion of inter-sectoral action for health as well as the synergistic impact of various interventions targeting more than one vector-borne disease where this is feasible (WHO 2004a). Whereas a number of countries in the African, Asian and the Eastern-Mediterranean regions of WHO are now adapting this strategy, there is still a lot to be done to ensure an effective integration of vector-borne disease programmes in each country (WHO 2001; 2004b).

Generally speaking, the integration of genetically modified mosquitoes into current vector control programmes will be faced with problems that are inherent to any conventional control tool, be it indoor residual spraying (IRS) or the use of insecticide-treated bednets (ITNs) (De Savigny 2004). As hinted above, the problem does not relate to the tools but, rather, the availability of a vector control system already in place to deliver the control tools in an alternative and sustainable manner. This includes strengthening of institutional, human and technical capacity at country level.

Specific challenges with respect to genetically modified mosquitoes

Before the integration of genetically modified mosquitoes into control programmes can be considered, there are still some important challenges and risks that need to be addressed. These include the unanticipated phenotypic changes resulting from transgenic alteration by effector genes and drive systems in a wild population and the unanticipated epidemiological impact/effects of control programmes (Alphey et al. 2002). There is indeed no proven technique to drive a ‘refractory construct’ into a field population, and this area requires further investigation. Moreover, both epidemiological and entomological risks must be assessed separately before releases can be performed (Benedict and Robinson 2003).

For early testing of mating competitiveness of transgenics, radiation sterilization may be used as a precaution against any unforeseen harmful effects of transgenic mosquito releases (Krafsur 1998). If and when questions about competitiveness and harmful effects have been resolved it will be necessary to proceed to non-sterilized mosquito releases to initiate the spread of transgenes in wild populations.

The introduction of transgenics to areas where other control measures such as ITNs and IRS are in place, might be thought to pose a problem. There is evidence from the field that male anophelines enter houses and would be vulnerable to killing by ITNs or IRS (Marchand 1985). However, this could only compromise the impact of the release technique where integration is proposed if, for some reason, the insecticidal method had proportionately more effect in killing the released males than the wild males. Such an effect does not seem very likely but should be considered.

Whereas current global initiatives are being explored on how best to apply laboratory advances in the field, conventional vector control programmes have many of the appropriate skills and facilities to participate in a vector control programme using genetically modified mosquitoes. The requirement for successful application of this method is indeed the ability to deliver to the field, over large areas, large numbers of sexually active genetically sterile males. Which control programme has such capacity?

If transgenics are to be integrated with conventional control it is essential that reliable data are available on the effects of the conventional control methods so that the additional effects of the transgenics can be accurately assessed. It may be noted that in earlier trials of genetic control, larvicides were used to attempt to create barrier zones around release areas in order to minimize the effects of immigration. Such procedures may also be necessary with trials of transgenics unless these focus on distinct and geographically or ecologically isolated populations.

Strengthening the capacity of control programmes

Vector control programmes intending to include genetically modified mosquitoes as one of the control options need to ensure the following:

1. A national vector control focal point with a broad understanding of vector control tools and basic entomology and ecology.
2. The vector control focal point must be supported by a core group of experts, either available within the control programme, or available within national research and academic institutions. This group will be responsible for the implementation of this method and for monitoring and evaluation of impact and potential risks.
3. In mosquito-borne disease-endemic areas earmarked for control using genetically modified mosquitoes, there must be facilities for the large-scale rearing of mosquitoes (insectaries and field laboratories).
4. An accurate assessment of the availability of reliable data on the effects of the conventional interventions and the additional effects of the transgenics is needed.
5. The integration of these new advances to currently weak health systems will require coordination and support from both national and international entities.

Conclusions

Most national vector control programmes are still struggling to effectively deliver conventional control tools/interventions such as the indoor residual spraying of houses with insecticides or the use of insecticide-treated bednets. Integrating the application of genetically modified insects (mosquitoes) with the current control programmes would require the general strengthening of the health system through IVM. To achieve this would need, among other things, additional resources – human, technical, financial and physical infrastructures.

References

Alphey, L., Beard, C.B., Billingsley, P., et al., 2002. Malaria control with genetically manipulated insect vectors. *Science*, 298 (5591), 119-121.

Benedict, M.Q. and Robinson, A.S., 2003. The first releases of transgenic mosquitoes: an argument for the sterile insect technique. *Trends in Parasitology*, 19 (8), 349-355.

Coluzzi, M. and Costantini, C., 2002. An alternative focus in strategic research on disease vectors: the potential of genetically modified non-biting mosquitoes. *Parassitologia*, 44 (3/4), 131-135.

De Savigny, D., 2004. Health systems and malaria: some perspectives, trends, and implications for malaria vector control and personal protection. *In: Proceedings of WHO Study Group on Malaria Vector Control and Personal Protection, March 2004, Geneva, Switzerland*.

Krafsur, E.S., 1998. Sterile insect technique for suppressing and eradicating insect population: 55 years and counting. *Journal of Agricultural Entomology,* 15 (4), 303-317.

Marchand, R.P., 1985. A new cage for observing mating behavior of wild *Anopheles gambiae* in the laboratory. *Journal of the American Mosquito Control Association,* 1 (2), 234-236.

Moreira, L.A., Ghosh, A.K., Abraham, E.G., et al., 2002. Genetic transformation of mosquitoes: a quest for malaria control. *International Journal of Parasitology,* 32 (13), 1599-1605.

WHO, 2001. *Workshop on a framework for the development and implementation of vector control interventions in the African region: final report, Harare, 6-9 February 2001*. World Health Organization, Regional Office for Africa, Harare, AFR/VBC/01.1. [http://www.afro.who.int/ddc/presentations/wkshp_interventions.html]

WHO, 2004a. *Global strategic framework for integrated vector management*. World Health Organization, Geneva, WHO/CDS/CPE/PVC/2004.10. [http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_PVC_2004_10.pdf]

WHO, 2004b. *Integrated vector management: strategic framework for the Eastern Mediterranean region 2004–2010*. World Health Organization, Regional Office for the Eastern Mediterranean, Cairo. [http://www.emro.who.int/rbm/ivm2004.pdf]