Despite very significant increases in funding aimed at reducing the incidence of malaria, WHO has recently reported that the declining trend in cases has levelled off. In 2017, the 10 highest burden countries in Africa reported a combined increase of over 3.5 million cases of malaria [1]. Much emphasis has been placed over the last two decades on increasing the use of insecticide treated bed nets, and indoor residual spraying (IRS) is still carried out in many areas, although not always as well as using a bed net. The widespread resistance of mosquitoes to the pyrethroids used in the fabric of these bed nets, as with the DDT sprayed on walls, was inevitable, especially given the lengthy persistence of these insecticides. This has been recognised as a major problem and recent efforts have been directed at using insecticides with a different mode of action including the synergist piperonyl butoxide in pyrethroid-treated nets to counteract the widespread resistance to pyrethroid insecticides. Similarly, new IRS pesticide compounds have been introduced into the market recently to combat resistance to pyrethroids.

Perhaps it is a suitable time to look back at the way control of the mosquito vector (Anopheles spp.) has been tackled over the centuries, and especially in the last few decades. Bed nets date back centuries, with an early observation of their use in Egypt by Herodotus (c440 BC) and in Asia, but once the vector of malaria was identified, much more attention was given to drainage projects to reduce breeding sites, such as the drainage of the Pontine Marshes in Italy in the 1930s. Larvicides such as Paris Green were applied, one example being in N.E. Brazil when An. gambiae was identified as an invasive species from Africa [2].

Effective control of the vector really begins in the 1940’s with the availability of DDT and successful implementation of residual spraying in Sardinia [3]. WHO then set up The Global Malaria Eradication Program which focussed on spraying the inside of houses. Teams of spray operators were recruited to travel to villages, like a military operation, and spray walls of houses - Indoor residual spraying (IRS). The effect was highly significant with many mosquitoes repelled and not entering treated houses, but those that did were killed when they rested on the treated walls. Mortality continued over a period of several months after treatment due to the persistence of the DDT spray deposits on mostly mud walls. In those days, people remained much more inside their houses after sunset, with the majority of transmission occurring indoors. As a result, the incidence of malaria fell rapidly. However, it was soon apparent that the mosquitoes were becoming resistant to DDT. This coupled with countries not willing to continue investment once initial reductions in malaria had been achieved resulted in WHO terminating the eradication programme.

The next phase of attempting malaria control on a Global scale was when bed nets were treated with insecticide, initially by soaking a net with an insecticide mixed with water. Due to the complexities in the logistics of re-treating nets every 6 months and concern about the villagers being exposed to the insecticide while treating the nets, the long-lasting insecticide treated net (LLIN) was commercially developed by adopting factory impregnation of nets with a pyrethroid, prior to their distribution and sale through health centres and aid agencies. The first such net was Sumitomo Chemicals Olyset™ Net. In the past ten years well over a thousand million of these nets have been distributed, but as Killeen et al. [4], pointed out “LLINs and IRS are highly effective in low and middle-income countries, but are insufficient to eliminate malaria transmission in many settings because of operational constraints, mosquitoes that behaviourally avoid contact with them inside houses and growing resistance to available insecticides.”

The use of any new insecticides with different modes of action, when developed, will need careful management to minimise the period of exposure to deposits whether on walls or in nets. However, we need to examine again the environment in which people live in malarious areas. The availability of electricity (both mains and solar powered) has expanded so some villages do have lighting, and with movement of people to urban areas, many no longer hide away in their houses at sunset, but are outdoors, often shopping or socialising late in the evenings when it is cooler. Undoubtedly outdoor biting will have increased. In a short assessment of the impact of supplying treated bed nets to a group of villages in Cameroon, it was clearly shown that although the number of cases of malaria did decrease, the greatest benefit of the LLINs was for children under 5 years of age, as they stayed under a net throughout the night, when the Anopheles vectors are most active [5].

Concern about the widespread resistance of mosquitoes to the available insecticides led to the formation of the Innovative Vector Control Consortium (IVCC)* which working with Syngenta, one of the agrochemical companies, has examined an
older insecticide, pirimiphos methyl, by using an encapsulated formulation to improve its persistence on wall surfaces, but there are now some new actives being developed. The first such IRS product is a neonicotinoid - clothianidin, the first totally new mode of action chemistry for IRS in over 40 years, which has recently been approved by WHO [6].

Space spraying is essentially the application of a cold fog with a very large number of small droplets (<30µm) of a non-persistent insecticide, and has been recommended to control Aedes aegypti, the vector of dengue virus and more recently Zika virus. This is usually only when there is an epidemic and the number of people affected has increased significantly so there was an urgent need to decrease the vector population. Too often it was a single treatment so after a significant drop in the mosquito population, it then increased very quickly as space treatments have no direct impact on larvae or pupae.

The majority of trials on space spraying often failed to include sequential treatments at short intervals to kill adult mosquitoes emerging from breeding sites after the first spray. Immigration can also occur rapidly from outside the treated area [7]. In consequence without the sequence of space sprays, the population of mosquitoes will rebound. Due to the lack of properly designed space spray trials, a recent Cochrane review of space treatment against malaria [8] was unable to estimate an effect of space spraying that was independent from temporal trends. In reality, if outdoor biting is to be reduced, space treatments are an essential component of integrated vector management. Space treatments would fill an important gap to achieve the malaria elimination goal. Only recently have small-scale trials been conducted in west Africa to determine the impact of a space treatment on swarms of mosquitoes [9,10], but more extensive randomised controlled trials in urban and village environments in Africa are urgently needed to confirm that the sequential aerosol spray technique is effective, if organised on a large scale [11].

In contrast, in the USA space treatments, usually applied at ultra-low volume (ULV) with both vehicle-mounted equipment and aerial treatments, are the principle means of keeping nuisance mosquito populations in check [12]. In 2016 aerial space treatments with the insecticide Naled were applied immediately in a distinct area of Miami-Dade County, Florida as well as larval treatments, when a case of Zika virus was detected to prevent spread of the virus. This quick response had an immediate effect on reducing the risk of the virus spreading [13].

In Africa following early studies in the 1950s, aerial ULV sprays have been used extensively against locusts and tsetse flies, the latter being controlled by aerial application of an aerosol [14]. With modern guidance systems, sequential aerosol treatments have been successful [15] and even at night against tsetse flies [16].

While scientists are actively doing research on genetically modifying mosquitoes to result in an all-male population that then crashes [17] and significant results have been achieved releasing mosquitoes with a dominant lethal (RIDL) gene [18], such techniques may require, in my opinion, a pre-treatment with a cold fog to reduce the natural population and minimise the number of genetically engineered mosquitoes that will need to be released.

However, much more attention is also needed in tropical areas to adjust current systems of mosquito control. Indoor residual spraying by spray teams should perhaps be devolved to local communities to reduce the costs of moving teams around the country, especially as villagers prefer someone living in their locality, whom they know, to enter their house to spray. At present an IRS treatment may be applied several weeks before the onset of the rains, so if IRS is carried out by villagers, the IRS could be implemented closer to when rainfall occurs after the long dry season. Larviciding has been considered, but with different species of Anopheles in an area, detection of all the possible breeding sites is considered to be extremely difficult.

In the highly populated urban areas greater priority is needed to do trials on space treatments to reduce outdoor biting. Accurate timing of such sprays using vehicle mounted equipment or aircraft, is needed especially in areas where mosquito populations increase rapidly once rainfall occurs at the commencement of the wet season. One advantage of using a low dose sequentially as a space treatment is that the insecticide is not persistent, so selection of resistance should be significantly less, especially if different modes of action can be managed by rotation between districts. The low dose present in a space spray for a very short period also minimises the risk of any potential impact on the environment. Such data showing a significant impact on malaria is needed to convince WHO and the Vector Control Advisory Group (VCAG) to allow space sprays as a part of an integrated vector management programme in the quest for elimination of malaria.

REFERENCES

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IVCC is a not-for-profit public-private partnership that was established as a charity in 2005.