***Aedes aegypti*, the principal mosquito species that transmits the Zika, dengue, and chikungunya viruses, has a number of breeding and behavioural quirks that make it extremely difficult to control.This article looks at conventional and new techniques for control and summarizes WHO guidance.**

The possibility that a mosquito bite during pregnancy could be linked to severe birth defects in newborns has alarmed the public and astonished scientists. Detection of an upsurge in cases of microcephaly, associated in time and place with Zika virus circulation, has been accompanied by findings of additional congenital malformation of the brain, detected in fetuses (by ultrasound), stillbirths, and newborns, and evidence of damage to eyesight and hearing. For women of childbearing age living in or visiting affected countries, the prospect of giving birth to a baby with such severe defects is terrifying.

The association of virus circulation with an increased detection of Guillain-Barré syndrome adds to the concern. GBS is an autoimmune disorder with various causes, including infections with some viruses and bacteria, most commonly Campylobacter jejuni. To date, an association between Zika virus circulation and an increased incidence of GBS has been reported in 8 countries: French Polynesia, Brazil, El Salvador, the French territory of Martinique, Colombia, Suriname, the Bolvarian Republic of Venezuela, and Honduras. In some of these countries, the fact that Zika is the only circulating flavivirus adds weight to this presumed association. Even in countries with advanced health systems, around 5% of patients with the syndrome die, despite immunotherapy. Many require treatment, including ventilatory support, in an intensive care unit, sometimes for months up to a year, adding to the burden on health services.

If these presumed associations are confirmed, the human and social consequences for the over 30 countries with recently detected Zika outbreaks will be staggering.

In the large outbreaks that affected some Pacific island nations, first in 2007 and again in 2013-2014, and then spread to the Americas, Zika virus has frequently co-circulated with dengue and chikungunya viruses. These viruses cross-react in diagnostic tests, making test results unreliable and putting better tests at the top of the list of most-needed new medical tools. Moreover the currently available PCR test can detect infection only during the period of illness when the virus is replicating, a weakness further compounded by the fact that 80% of infections cause no symptoms. Although at least 15 groups are working on Zika vaccines, WHO estimates that it will be at least 18 months before vaccines could be tested in large-scale trials.

For all these reasons, WHO recommends stepped-up personal and population-wide measures for mosquito control as the best immediate line of defense.

Aedes aegypti: an “opportunistic” and tenacious menace

Aedes aegypti is the principal mosquito species that transmits Zika, dengue, chikungunya, and yellow fever to humans. More than half of the world’s population lives in areas where this

mosquito species is present.

Experts describeÂ *Aedes aegypti* as “opportunistic”, as it shows a remarkable ability to adapt to changing environments, especially those created by changes in the way humanity inhabits the planet. Over the years, it has exploited these opportunities, which include phenomenal increases in international travel and trade and rapid unplanned urbanization, with striking efficiency. Most ominously,Â *Aedes aegypti*mosquitoes, which long bred in water collected in tree holes and the axils of plant leaves in forests, have adapted to breed in urban areas, flourishing in impoverished crowded areas with no piped water and poorly collected garbage and trash.

These adaptations classify theÂ *Aedes aegypti* species as a “container breeder”. The mosquitoes can breed wherever rain collects or water is stored, with preference for outdoor breeding sites. Larvae have been found in a host of artificial containers, like discarded plastic cups and bottle caps, plates under potted plants, birdbaths, vases in cemeteries, and water bowls for pets. The mosquitoes can also breed in the microbial stew found in septic tanks, toilet tanks, and shower stalls. Construction sites, used tyres, and clogged rain gutters offer additional opportunities to breed in large numbers.

Laid eggs can survive for very long periods of time in a dry state, often for more than a year. Once submerged in water, they hatch immediately. If temperatures are cool, mosquitoes can remain in the larval stage for months so long as the water supply is sufficient. The eggs are sticky, virtually gluing themselves to the insides of containers. International trade in used tyres is the best documented vehicle for introducing the mosquito to distant places.

Females: aggressive biting and “sneak attacks”

Aedes aegypti is an aggressive daytime biting mosquito. Only the females bite. Biting is most intense in the hours around dawn and dusk. Indoors, the mosquitoes can bite at night in well-lit homes. They are adept at hiding in closets and under beds. Adult mosquitoes of both sexes feed on sweet things, like nectar and fruit, but females need the protein in blood to develop their eggs.

Over the years, females have evolved to show distinct preferences: for human blood over that from other mammals, for shady resting places, for stagnant as opposed to fresh water, and for small artificial containers as the best place to lay their eggs, with this last preference extending to dark-coloured containers as opposed to lighter-coloured ones. Females often use “sneak attacks”, approaching victims from behind and biting on ankles and elbows, which likely protects them from being noticed and getting slapped.

Aedes aegypti females are so-called “sip feeders”. Instead of drawing sufficient blood for a meal in a single bite, they take multiple little sips during multiple bites, thus increasing the number of people a single mosquito carrying the virus can infect.

After a blood meal, females produce an average batch of 100 to 200 eggs, depending on the size of the blood meal. Unlike most other mosquito species, a femaleÂ *Aedes aegypti* can

produce up to 5 batches of eggs during her lifetime. As yet another survival tactic, a single female lays her batches of eggs at several different sites.

All of these features makeÂ *Aedes aegypti* populations extremely difficult to control. They also make the diseases they spread a much larger menace.

The rise and fall of mosquito control

After the discovery and effective use of residual insecticides in the 1940s, large-scale and systematic control programmes succeeded in bringing most of the important mosquito-borne diseases under control in many parts of the world.Â *Aedes aegypti* was virtually eliminated from the Americas. By the late 1960s, most mosquito-borne diseases were no longer considered to be major public health problems outside Africa.

As so often happens in public health, when a health threat subsides, the control programme dies. Resources dwindled, control programmes collapsed, infrastructures dismantled, and fewer specialists were trained and deployed. The mosquitoes – and the diseases they transmit –roared back with a vengeance. They returned to an environment with few defences left intact. Nearly 2 decades of diminishing interest and dwindling expertise severely weakened national capacities to implement programmes for mosquito control. Previously successful control programmes were replaced by the reactive space spraying of insecticides during emergencies, a measure with high visibility and political appeal but low impact unless integrated with other control strategies.

The weakness – sometimes disappearance – of control capacity coincided with trends, like accelerating population growth, rapid unplanned urbanization, and changes in patterns of land use, which made environments even more hospitable for flourishingÂ *Aedes aegypti* populations. In addition, the arsenal of effective insecticides shrank as mosquitoes developed resistance.

The consequences of this dramatic comeback are best illustrated by the recent history of dengue. Compared with the situation 50 years ago, the worldwide incidence of dengue has risen 30-fold. More countries are reporting their first outbreaks. More outbreaks are explosive in ways that severely disrupt societies and drain economies. The continuing increase in dengue outbreaks prompts some experts to ask: if countries cannot defend themselves against disruptive and recurring outbreaks of a well-known disease like dengue, what hope is there that mosquito control will help stop Zika?

WHO advice: conventional and newer tools for mosquito control

WHO has issued advice on mosquito control as part of the response to Zika virus disease. As noted, well-implemented mosquito control can effectively reduce the transmission of mosquito-borne viruses, including Zika. However, mosquito control is complex, costly, and blunted by the spread of insecticide resistance. Few developing countries outside sub-Saharan Africa have dedicated well-funded programmes for mosquito control. Moreover, some control measures are not readily accepted by the public.

Integrated approaches that tackle all life stages of the mosquito and fully engage communities are recommended. Although fogging to kill adult mosquitoes provides the most visible evidence that a government is taking action, WHO stresses that the elimination of mosquito breeding sites is the most effective intervention for protecting populations. Fogging, which is recommended for emergency situations only, is most effective when conducted in the hours around dawn and dusk, when mosquito activity is most intense. Measures for personal protection against mosquito bites, including repellents that are safe for use during pregnancy, are also covered.

Given the seriousness of the dengue and now the Zika crises and the need for a broader range of control techniques, a WHO Vector Control Advisory Group has evaluated some newer tools, including a genetically modified prototype mosquito submitted for WHO review. For genetically modified mosquitoes, the WHO Advisory Group has recommended further field trials and risk assessment to evaluate the impact of this new tool on disease transmission. Trials previously conducted in the Cayman Islands showed significant reductions in the Ae. aegypti population.

Another technique being developed involves the mass release of male insects that have been sterilized by low doses of radiation. When sterile males mate, the female's eggs are not viable, and the insect population dies out. The sterile insect technique has been successfully used, on a large scale, by the International Atomic Energy Agency and FAO to control agriculturally important insect pests.

A promising biological method of control uses male mosquitoes carrying the naturally occurring Wolbachia bacteria, which are found in 60% of common insects, including butterflies and fruit flies. These bacteria do not infect humans or other mammals. When females mate with males carrying the bacteria, the eggs do not hatch, thus suppressing mosquito populations. Another strain of Wolbachia under investigation establishes the bacteria in the mosquito population and reduces the mosquitoes' ability to transmit dengue. The mosquitoes are not genetically modified as the technique involves no tampering with or modifications of genes. Mosquitoes carrying Wolbachia bacteria have been released in several places, including Australia, Brazil, Indonesia, and Viet Nam as part of control strategies for dengue. Large-scale field trials of Wolbachia bacteria will be initiated soon.

Some countries affected by Zika are using biological methods as part of an integrated approach to mosquito control. El Salvador, for example, with strong support from fishing communities, is introducing larvae-devouring fish into water storage containers.

Given the magnitude of the Zika crisis, WHO encourages affected countries and their partners to boost the use of both old and new approaches to mosquito control as the most immediate line of defence.