The fight against dengue: Mainstays and updates

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Controversy erupted late 2014 when clinical trials for aspiring antidengue drug ActRx TriAct were halted due to concerns that researchers had bypassed scientific, regulatory and ethical safeguards. ActRx TriAct – a compound of artemether, artesunate and berberine – had initially been tested in dengue patients at Ospital ng Palawan and San Lazaro Hospital and slated for further testing at other government hospitals. However, procedural irregularities prompted the Department of Health (DOH) to suspend the trials, a move supported by the WHO and local physician groups. A critical issue noted by DOH was that use of ActRx TriAct could lead to drug resistance against artemisinin, the only effective treatment against the deadly *Plasmodium falciparum* malaria. Citing a WHO technical opinion, DOH noted that berberine did not have established therapeutic effects versus mosquito-borne diseases, while artemether and artesunate are both derivatives of the antimalaria drug artemisinin. Functionally, therefore, the ActRx TriAct drug combination constituted a form of artemisinin monotherapy, which has been linked to antimalarial drug resistance and thus strongly discouraged by the WHO.

While that search for an effective antidengue treatment has met a roadblock here in the Philippines, prevention and control efforts continue to be carried out on the community level.

Vector control: ingenious mosquito traps

A mosquito ovicidal-larvicidal (OL) trap system – consisting of a black-painted can, a strip of lawanit board and a black pepper solution – was developed by researchers from the Department of Science and Technology with the goal of reducing mosquito density and dengue virus transmission.[1] Black pepper pellets are dissolved in water inside the can then the lawanit board is placed in the solution with its rough surface facing up. The solution moistens the board, attracting female *Aedes* mosquitoes to lay eggs on the board, where the solution then kills the eggs and the larvae. Field tests report 86.2% egg and larval mortality rate.[2] The OL traps have also become useful for surveillance of mosquito populations in communities where they have been deployed, as well as in raising dengue awareness and sense of responsibility, particularly in community members who are tasked to monitor the traps.

A do-it-yourself alternative mosquito trap uses water, yeast, brown sugar and a plastic bottle covered in black paper. The upper portion of the bottle is cut, inverted and fitted back in, creating a funnel that partially covers the bottle. A solution of water, yeast and brown sugar is poured into the container; the carbon dioxide emitted by the mixture attracts mosquitoes, which are then trapped inside the bottle.

Environmental management is still mainstay of dengue control

Other vector control solutions[3, 4] that have been implemented or considered over the years include:

- Larvivorous fishes such as gambusia and guppies
- Predatory copepods (small freshwater crustaceans) such as native water bugs
- Release of genetically modified male mosquitoes into the environment, where the mutation is transmitted to female mosquitoes during mating and disables a muscle that renders the females flightless
- Chemical larvicides and adulticides
- Space spraying, recommended only in emergency situations to suppress an ongoing epidemic or prevent an incipient one

The mainstay of dengue vector control, however, is still environmental management – frequent emptying of water containers, regular cleaning, installation of mosquito screens and use of mosquito nets while sleeping, fumigation, among others.

At the frontiers of the fight against dengue

As early as this year, the world could see the release of the first dengue vaccine (CYD-TDV). Additional vaccine candidates are in clinical development; two are expected to begin Phase III trials in 2015-2016. New discoveries – such as that of the critical role of DENV nonstructural protein 1 in vascular leakage[5] – continue to propel our understanding of how the disease can be combatted. Hand in hand with proven community-based solutions, a turning point in the fight against dengue could be forthcoming.

Resources: 1. DOST resources page. Department of Science and Technology website. Available at: http://www.dost.gov.ph/index.php/knowledge-resources/news/37-2010-news/323-dost-brings-anti-dengue-fight-right-where-it-starts. Accessed 15 October 2015. **2.** Briones AV, Garbo AG, Casa EP, et al. Field Testing of Ovicidal-Larvicidal Trap System with Pelletized Extracts of Piper nigrum L. for Aedes Mosquito in Quezon City and Marikina City. *Acta Med Philipp*. 2013;47(2). Available at: http://actamedicaphilippina.com.ph/content/field-testing-ovicidal-larvicidal-trap-system-pelletized-extracts-piper-nigrum-l-aedes-mosqu. Accessed 15 October 2015. **3.** PCHRD resources page. Philippine Council for Health Research and Development website. Available at: http://www.pchrd.dost.gov.ph/index.php/news/dengue-updates. Accessed 15 October 2015. **4.** WHO resources page. World Health Organization website. Available at: http://www.who.int/denguecontrol/control_strategies/en/. Accessed 15 October 2015. **5.** Beatty PR, Puerta-Guardo H, Killingbeck SS, et al. Dengue virus NS1 triggers endothelial permeability and vascular leak that is prevented by NS1 vaccination. *Sci Transl Med.* 2015 Sep 9;7(304):304ra141. Available at: http://stm.sciencemag.org/content/7/304/304ra141.abstract. Accessed 15 October 2015.