

EVOLUTION OF DENGUE CONTROL STRATEGIES IN NORTH QUEENSLAND, AUSTRALIA.

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DENGUE CONTROL IN NORTH QUEENSLAND: THE BIRTH OF THE DENGUE FEVER MANAGEMENT PLAN

A large outbreak of dengue virus type 2 (DENV-2) in 1992-93 affected several north Queensland communities, and would serve as the trigger for the development of comprehensive dengue control strategies by Queensland Health. The outbreak hit especially hard in Townsville and Charters Towers. Townsville recorded nearly 1000 cases (Streatfield et al. 1993) while up to 27% of the population of Charters Towers was exposed to the virus (McBride et al. 1998). This large outbreak, coming after the end of the Commonwealth-sponsored dengue "Mosquito Eradication Campaign" of the mid 1980s (Kay 1986), struck home the fact that dengue had to be taken seriously in north Queensland, a point originally made by Kay et al. (1984) after the 1981 dengue outbreak in the Torres Strait. In response, Queensland Health, in collaboration with local stakeholders and international experts, including Dr. Duane Gubler of the US Centers for Disease Control, formulated the first Dengue Fever Management Plan (DFMP) for north Queensland (Ritchie et al. 2002). This plan incorporated disease surveillance, health education and mosquito surveillance and control to form a comprehensive dengue control program.

Initially, the DFMP was successful, limiting an outbreak of DENV-2 in the Cairns suburb of Manunda to only 4 cases (Ritchie et al. 1995). However, a large outbreak of DENV-2 in the Torres Strait (Fig 1) that affected several islands and ultimately spread to Cairns exposed the Achilles Heel of the DFMP: delay in recognition or notification of cases. The 1996-97 Torres outbreak (Hanna et al. 1998) began the last week of October 1996 after a woman returned to Murray (Mer) Island after visiting Papua New Guinea. The women had dengue, and subsequently local transmission started on Murray. The Tropical Public Health Unit (TPHU) was not notified of dengue until the 1st week of December. By this time, the outbreak was in full swing on Murray, and soon spread to Darnley (Erub) and Yorke (Masig) islands before eventually creating havoc on Thursday Island. It also led to a small outbreak in Cairns. The outbreak was notable for several reasons: 1. it demonstrated the consequences of delays of notification of dengue; 2. It demonstrated how dengue can rapidly move between Torres Strait islands, particularly during the Christmas holidays (this so-called "Christmas Rush" has resulted in the jumping of dengue outbreaks during other outbreaks in north Queensland, notable the 2003-04 Torres Cairns DENV-2 outbreak); and 3. It was the first time that interior spraying using synthetic pyrethrins had been successfully used to stop dengue transmission on Yam (Iama) and Darnley islands, and during the Cairns outbreak.

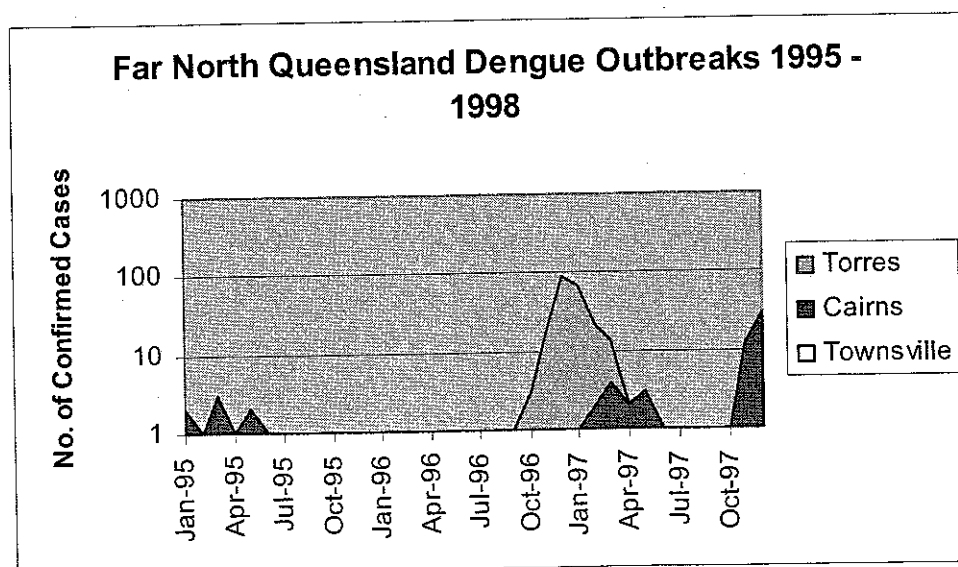


Figure 1. Dengue outbreaks in north Queensland, 1995-1998; monthly confirmed cases in log scale.

It was nearly a year later than an outbreak of DENV-3 virus (Hanna et al. 2001) would redefine the DFMP for north Queensland. In early December 1997, an outbreak of an especially virulent DENV-3 virus began along the Cairns Esplanade. At the time, the TPHU dengue team consisted of a medical entomologist (Scott Ritchie) and a vector control officer, Andrew van den Hurk. Thus, when this outbreak moved into several other suburbs, and explosive transmission began in older parts of Parramatta Park, the TPHU staff was overwhelmed. Environmental Health Officers from Cairns City Council (CCC), along with TPHU staff managed to keep the outbreak under control (Fig 2) but were unable to eliminate it. The critical time for eradication of the virus was probably in March/April 1998, when dengue was eliminated from Parramatta Park and was restricted to the beach suburbs of Holloways Beach and Machans Beach. However, at this time Japanese encephalitis virus (JEV) activity was detected on the Australian mainland, and the TPHU medical entomology staff was diverted to investigate this outbreak (Hanna et al. 1999). Despite an infusion of emergency "non-specialist" dengue control staff by the CCC, dengue activity persisted in Machans Beach and then spread to Port Douglas in June. Warm weather, an unseasonable late August rain storm, and a plethora of large breeding containers led to explosive transmission in the town of Mossman after the virus was introduced from Port Douglas. In October 1998, unprecedented levels of dengue transmission occurred in the Cairns region, with 68 and 86 cases reported in October and November, respectively, primarily in Mossman.

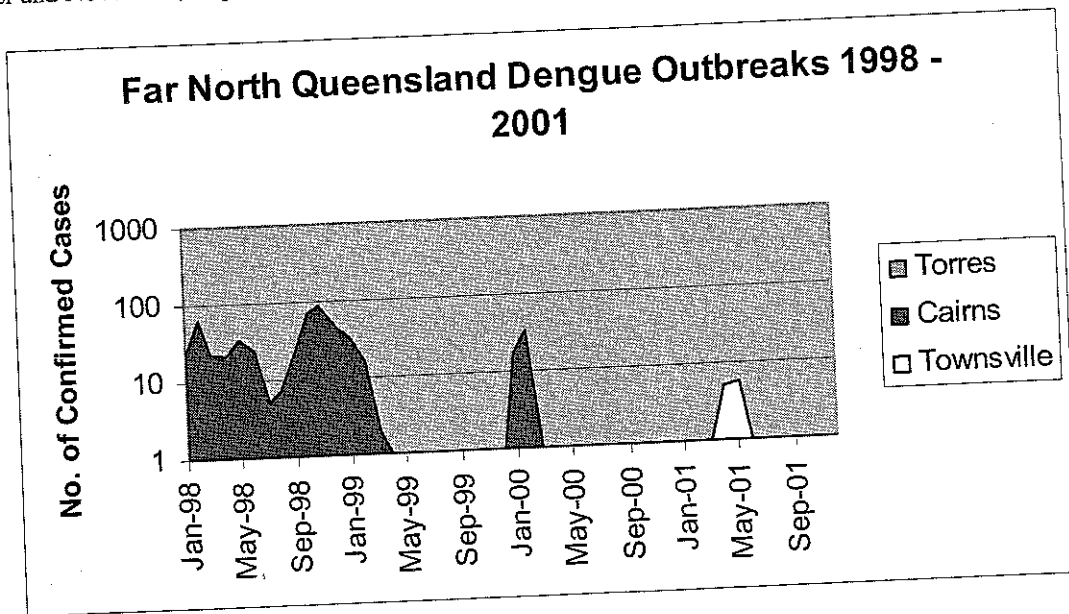


Figure 2. Dengue outbreaks in north Queensland, 1998-2001.

It was at this time that Queensland Health (QH) decided to fund a specialist team whose responsibility was primarily dengue control. The Dengue Action Response Team (DART) was on the ground in December 1998, and by March 1999, the long outbreak of DENV-3 that had caused 498 cases, 100 hospitalisations and affected 15 different areas, was over. More than anything, this outbreak stressed that dengue control required skilled staff that could thoroughly eliminate *Aedes aegypti* (L.) breeding sites while providing a comprehensive interior spray campaign in affected suburbs.

THE NEW 2000 DFMP: THE DART ROLLS

The success of the DART was due to several factors (Ritchie et al. 2002). The specialised approach allowed the staff to develop unique skills for efficient, effective dengue control. In particular, the DART developed the ability to locate cryptic breeding sites (Russell et al. 2002), honed communication skills to convince residents to allow the DART to spray inside their homes to control dengue mosquitoes, and developed the expertise to use palm-based computers and Geographical Information Systems to collect data and map cases/responses. A revised DFMP was launched after a meeting similar to the 1994 meeting that led to the development of the original DFMP. Key elements of the new DFMP were the necessity for early case recognition and notification (Malcolm et al. 1999), the utilisation of the specialist DART, the incorporation of thorough interior spraying using residual synthetic pyrethrins to treat *Ae. aegypti* harbourage sites within the home (Ritchie et al. 2002) and the treatment of roof gutters, a highly productive breeding site (Montgomery and Ritchie 2002), with s-methoprene pellets.

The new DFMP was highly successful (Fig 2). Despite the fact that the number of imported cases and, indeed, outbreaks had increased, the total number of dengue cases dropped from 722 from 4 outbreaks in 1995-2000 to 84 from 5 outbreaks in 2000-2002 (Ritchie et al. 2002). Early notification within a week allowed the DART and local council Environmental Health Offices (EHOs) to eliminate *Ae. aegypti* before they could become infected (the extrinsic incubation period of dengue virus is ca. 10 days during summer). This was also when the 100:200 rule became entrenched. All premises within 100 m of the case house were subject to larval control AND interior spraying by the DART; whereas premises from 100 – 200 m of the case house only received larval control, generally by local council workers.

This new effort was best exemplified by the 2000 DENV-2 outbreak in Machans Beach (Ritchie et al. 2001). Despite a relatively late notification of activity, during which 17 known cases had already been contracted, the outbreak was eliminated within 47 days, limited to 50 cases and, most importantly, did not escape to other areas. From this time on, 4 additional outbreaks of dengue would occur, including 2 in Townsville. All but one of these would be eliminated before they had spread beyond their point of origin, and none would total more than 21 cases. Furthermore, no dengue cases resulted from 8 imported dengue cases in returning personnel working in East Timor during the 1999-2000 E. Timor "event". The SWAT team, fire fighter system of "careful watch, decisive action" had proved enormously successful in preventing major dengue outbreaks.

THE GREAT DEN-2 EPIDEMIC OF 2003

In early 2003, the Christmas Rush would strike again. A nurse from Papua New Guinea arrived in Parramatta Park after having visited PNG over the holidays. Heavy rains earlier in January had hatched large broods of *Ae. aegypti*, and the old Queenslander houses of Parramatta Park were "alive" with them. The nurse, who was ill enough to be hospitalised, was initially diagnosed with malaria. It would not be until early March, 42 days after the nurse became ill, that the TPHU was notified of dengue in Parramatta Park. And thus was the start of the most explosive outbreak of dengue encountered since the 1992 Townsville epidemic. By the time the TPHU was notified of the activity in the area, we calculate that 89 cases had already been contracted. The DART were literally overwhelmed. In addition to epidemic dengue in Parramatta Park, cases started showing up in several other Cairns suburbs, and by May had spread to Townsville.

The DART, overwhelmed by the scale of the outbreak, were forced to apply a triage approach to interior spraying. The 100-200 rule was abandoned, with interior spraying sometimes restricted to the case and adjacent houses, or none at all, should the risk of *Ae. aegypti* seem small. For example, in new subdivisions with screened housing. And while dengue cases declined, new suburbs reported activity on an almost daily basis. Clearly, additional forces had to be employed. Local councils and QH staff used any available EHOs, and entomological/vector control staff as far away as New Zealand, Northern Territory and Western Australia pitched in. Eventually, the 2003 outbreak of DENV-2 ended, with the last transmission in July, after a total of 459 cases (Fig 3). The workload had been huge: 2,829 yards inspected and 1,646 premises sprayed, not to mention the extra staff that were employed by the TPHU to aid with data entry and patient interviews.

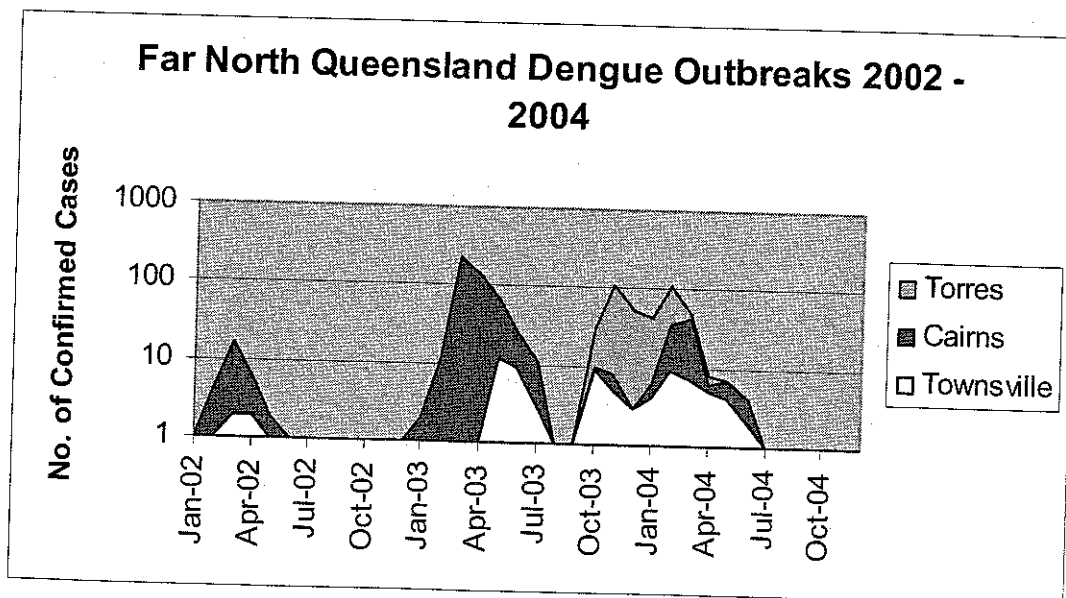


Figure 3. Dengue outbreaks in north Queensland, 2002-2004.

The 2003 Parramatta Park revealed the Achilles Heel of the “careful watch, decisive action” response plan. Basically, no matter how careful you were, dengue case could escape detection, leading to late notifications and local transmission. Clearly, more preventative *Ae. aegypti* control would have to be done in inter-epidemic periods to prevent explosive transmission. The outbreak also highlighted the vulnerability of the interior spraying approach. The high workload during the heat of summer, lugging a 10 kg Rega spray can through dog-infested yards, told on the DART. At one point, 2 of the 3 DART members were incapacitated by injury. Additionally, the use of large amounts of pesticide (1,646 premises were sprayed) exposed workers and the public to pesticides despite the use of personal protection equipment and judicious application. Finally, interior spraying is slow. It takes ca. 20 minutes for a 2 person team to inspect a yard and conduct interior spraying. On a good day, a team can complete 20 premises.

In response to the increasing caseload created by the epidemic and the laborious spray schedule, the TPHU fast-tracked development of a lethal ovitrap (LO) program. In 1999, Zeichner and Perich (1999) published laboratory studies indicating that ovitraps with velour “ovistrips” treated with residual synthetic pyrethrins could be used to kill *Ae. aegypti*. Studies funded by Queensland Health demonstrated that a variety of residual insecticides (deltamethrin, lambda-cyhalothrin, bifenthrin, fipronil) and even an adhesive could be used to kill from 77% to 93% of gravid female *Ae. aegypti* in 13 sq. m dome tent cages within 48 hr (Ritchie et al. unpublished data). Because mortality was similar among the pesticides, bifenthrin was chosen as the pesticide of choice owing to its low mammalian toxicity (the oral and dermal rat LD₅₀ is 632 mg/kg >2000 mg/kg, respectively), and its ability to adhere tightly once dried to a substrate (Lee et al. 2004).

STICKY AND LETHAL OBITRAPS, “LURE AND KILL”, HERALD A SOFT APPROACH TO DENGUE CONTROL

The move to a “lure and kill” approach to dengue control was basically one of expediency. We had always intended to develop “lure and kill” approaches; a grant to develop the method in north Queensland was submitted to the National Health & Medical Research Council (NHMRC) in 2003 (subsequently funded in 2004). But the overwhelming case load, coupled with the injuries, meant we had to find a dengue control strategy that was quicker than interior spraying and yet effective. The rationale behind “lure and kill” approach is simple: a lure, either a pheromone or kairomone, that is highly attractive to a specific insect, is mixed with a pesticide or presented in such a way that the attracted insects are killed (eg. Glue trap). Basically, a booby-trapped beer. Annihilation trapping, whereby the target area is flooded with a high density of lure and kill traps, has proven successful in the elimination of other insects, such as the papaya fruitfly in north Queensland in the late 1990s (see <http://www.dpi.qld.gov.au/health/4670.html>).

For *Ae. aegypti*, the infusion in an ovitrap is the lure. In larval control programs, the breeding site is either treated or turned over. In its place, LOs baited with an infusion attractant and a cloth strip treated with insecticide are used. By literally swamping the dengue treatment area with LOs, there is a high probability that ovipositing female *Ae. aegypti* will visit the trap. Furthermore, time is in our favour. From the time it takes a female *Ae. aegypti* to become infected after having taken a viraemic bloodmeal, ca. 10 days, she will have to lay eggs at least once, perhaps several times (developmental time from bloodmeal to eggs is ca. 4 days). Finally, there is evidence that *Ae. aegypti* visit several oviposition sites (Colton et al. 2003), increasing the likelihood that she will visit a LO. Ovitrap can also be “treated” with a sticky plastic insert to create a sticky ovitrap (SO) to collect gravid mosquitoes (Ritchie et al. 2003, 2004).

So, beginning in April 2003, the first operational use of LO during a dengue outbreak began. Interior spraying was still used, but only within a limited area, say the case house and adjoining premises. Full larval control using s-methoprene pellets, source reduction and aerosol lambda-cyhalothrin sprays was also conducted at most premises. Initial results were very encouraging. Using a variety of LOs (sticky, bifenthrin and a combination of the two), further dengue transmission only occurred in 2/14 (14%) of the interventions. And many of the interventions involved multiple cases. Of the 29 dengue cases responded to, only a further 5 cases occurred after control. The last seven interventions utilised a combination of SOs and LO.

Both LOs and SOs provide data that can be used to estimate the risk for ongoing dengue transmission. Because eggs are laid on the LO strip, the mean number of eggs and the percent of LO with eggs are a measure of container mosquito abundance. The proportion of SO collection consisting of *Ae. aegypti* provides an estimate of the abundance of *Ae. aegypti* (note, only aedine species that oviposit on an ovistrip, such as *Ochlerotatus notoscriptus* [Skuse] and *Oc. palmarum* [Edwards], are included in the calculation). For example, an intervention in response to 3 dengue cases at Freshwater (note: street names are fictitious for confidentiality) is summarised as follows:

- 2 cases at 10 Smith St, 1 at 13 Smith St;
- 58 premises in area, 48 inspected and received larval control;
- Only the 13 Smith St case house was sprayed inside with lambda-cyhalothrin;

- 14 glue traps set at 12 premises for 14 days;
- 28 bifenthrin traps set at 24 houses for 14 days;
- Glue traps collected 31 aedine mosquitoes, 7 (23%) of which were *Ae. aegypti*;
- Bifenthrin traps: 12/28 (43%) had a total of 149 eggs (mean = 5.3/LO) and
- No further dengue cases occurred.

Only 43% of the LO contained eggs, and the SO data suggest that most were not *Ae. aegypti*. The Sticky Ovitrap Index (SOI), the mean number of *Ae. aegypti* per SO/week, was only 0.5, below the potential dengue transmission risk level of 1 Ritchie et al. (2004) estimated from SOs set in Parramatta Park during the course of the 2003 DENV-2 outbreak. Thus, the risk of ongoing transmission in Freshwater was low. We have recovered significantly higher oviposition rates in many interventions, with up to 100% of LO with eggs, and a mean number of eggs/LO ranging from 1.3 – 73. These data certainly indicate that *Ae. aegypti* oviposit in LO, and bioassays from LO strips set in the field indicate that they kill. Red polyester velour strips, treated with Bistar 80 SC at the labelled rate of 12.5 ml/l, set in a LO for up to 4 weeks killed over 80% of the female *Ae. aegypti* in direct contact with the strip for only 1 minute (S. Ritchie, unpublished data). We are conducting further field and lab trials to quantify oviposition, repellency and lethality of LO to *Ae. aegypti* (Williams et al. 2005).

Dengue interventions using LOs offer several advantages over interior spraying campaigns. First, the amount of pesticide used is greatly reduced; each LO strip contains only 3.5 mg of 100% AI bifenthrin, whereas interior spraying uses 1000 – 10,000 mg per premise. Obviously, the difference in pesticide cost is significant. Exposure of nontargets to insecticide would obviously be less, especially to operators applying the insecticide and to insects and animals harbouring inside houses. Finally, efficiency is basically doubled. Based upon records of interventions conducted in 2003-2004, two teams of two workers, a typical response team during an outbreak, could treat 105 and 205 premises in a week when using interior spraying vs. lethal ovitrapping, respectively. Thus, considering the notification delay of 6 weeks that occurred in the Parramatta Park outbreak, only the use of LO would enable the DART to keep abreast of the outbreak (Fig 4).

2004: TOO MANY VARIABLES!

2004 started off with a bang. An outbreak of DENV-2 began in November on the Torres Strait island of Yam, and nearly killed two women who developed Dengue Haemorrhagic Fever (DHF). Again, a late recognition and notification of the outbreak allowed it escalate rapidly. Interior spraying was used to eliminate dengue from Yam, but not before it had spread to Thursday Island (TI). A large intervention, incorporating larval control, LO and limited interior spraying was used to eliminate dengue from TI (Montgomery et al. 2005), but not before the first death from DHF occurred. Concurrently, in February of 2004, a significant outbreak of DENV-2, likely introduced into Cairns from TI via the Christmas Rush, broke out in the industrial suburb of Bungalow in Cairns. To add insult to injury, DENV-2 flared up again in Townsville. Amazingly, it was the same virus that had affected Cairns and Townsville the previous year! Thus, the DART and TPHU had to fight dengue on three simultaneous fronts (Fig 4) in early 2004. In response to this multi-regional outbreak, QH has hired 3 additional DART, 2 based in Cairns serving Cairns and the Torres, and one based in Townsville.

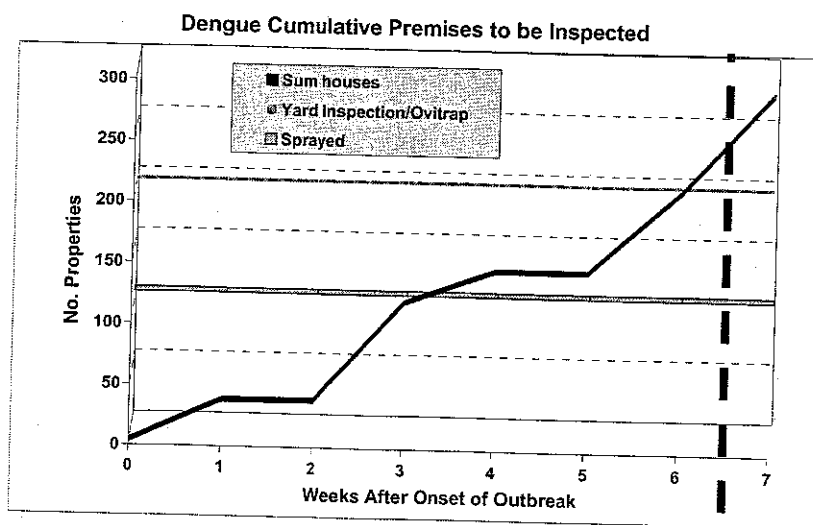


Figure 4. Cumulative number of premises requiring dengue control during the 2003 DENV-2 outbreak in Parramatta Park. Horizontal lines represent for the number of premises that 2 teams of 2 workers each could inspect and treat using interior spraying and lethal ovitraps (LO) are shown. Date of notification at the 6 week point (vertical dashed line) indicates that only use of LO would enable workers to “catch up” to the outbreak.

LO interventions were not as successful as in 2003. Of the 8 interventions in response to 10 dengue cases in 2004, breakout dengue transmission occurred in 4 (50%), with 11 total cases resulting after treatment. Why the high failure rate? Or, better put, was there any difference between 2004 and 2003 that explained the poor control? Clearly, the mitigating factor was a lack of thoroughness resulting in an insufficient number of yards inspected and, in particular, LOs set (Table 1). Mosquito abundance and the promptness of the response were almost identical in 2003 and 2004. In reviewing the individual responses, it was clear that a lack of manpower, created by the response to multiple dengue outbreaks in the Torres Strait, Cairns and Townsville, led to insufficient response by the DART in some cases, reflected in both the number of houses sprayed and LOs set. Thus, it is also possible that the poor results in 2004 may be due to fewer houses sprayed rather than receiving LO.

Table 1. Summary of factors likely to have influenced the efficacy of “lure and kill” dengue interventions in 2003 – 2004.

Factor affecting dengue control	2003 (n = 14)	2004 (n = 8)
Promptness in response (days from 1 st viraemic day until day traps set)	14	12
Vector abundance (mean <i>Ae. aegypti</i> /sticky trap, mean eggs/LO)	1.1, 10	1.1, 17
Thoroughness (No. premises treated by larviciding and LO in 100 zone)	74%	57%
Interior spraying (no, % premises sprayed)	10, 16%	3, 3%
Aggressiveness (No. LO placed in 100 zone)	44	21

Despite the reduced efficiency, the number of dengue cases did not increase, but rather persisted as a creeping outbreak, suggesting that some control was taking effect. Interesting, in 3 of the 4 interventions in 2004, 2nd transmission was due to multiple cases within a single house with nearly identical onsets, suggesting a single infected mosquito had negotiated the gauntlet of control measures. Ultimately, the Cairns, Torres and even the Townsville outbreaks were eliminated through the integrated use of LO, larval control and limited interior spraying.

“LURE AND KILL”: THE NEW MODEL FOR DENGUE CONTROL?

The lure and kill approach appears to be a worthy addition to our dengue control arsenal. LOs, by themselves, are unproven as a complete control strategy. Source reduction and larval control will likely need to be conducted to provide an extra level of control, and to enhance the attractiveness of the LO. Interior spraying is still the only way we have to target host-seeking mosquitoes, the biting mosquitoes involved in active dengue transmission, inside the house. But LO provide a persistent control targeting older, gravid mosquitoes that are likely to become, or already are, viraemic.

Lure and kill approaches are in their infancy, with significant work yet to come before they are fully operational. To improve the lure and kill approach, we hope to develop traps targeting host-seeking adults. Already, trials have been conducted using kairomones and new traps specific for *Ae. aegypti*, as developed by Martin Geier (Williams et al. 2005). New traps, such as the MosquiTRAP, a sticky ovitrap developed in Brazil, will be trialled. Field trials validating the method must be undertaken. Because LO target older mosquitoes, we will need to be able to estimate the chronological age of mosquitoes. Work currently underway by Leon Hugo at the Queensland Institute of Medical Research and Peter Cook at University of Queensland aims to provide biochemical and molecular techniques to do so. Ultimately, we will have a system employing both host-seeking and oviposition traps to improve surveillance and, most importantly, provide an efficient, environmentally-friendly technique to control *Ae. aegypti*.

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