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ScienceTalk

Act against dengue now with tools that exist

While more basic research is clearly needed, available methods can make a difference

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An NEA officer checking the roof of a house for mosquito-breeding sites. Vector control remains a key strategy in the fight against dengue. ST PHOTO: NG SOR LUAN

Sir Robert Watson Watt, one of the inventors of radar, once said: "Give them the third best to go on with; the second best comes too late, the best never comes."

In the public health arena we frequently, in our quest for perfection, lose sight of tools that we have in hand which can make a big impact on the multitude of public health problems we face. We also often forget that no single tool can solve these complex problems.

The control of dengue is a prime example. The incidence of dengue, caused by viruses spread by the Aedes mosquito, has increased 30-fold in the past 50 years.

An estimated 390 million cases occur every year in more than 100 countries, mostly in the developing world, and 40 per cent of the world's population is at risk. Each year, an estimated half a million people contract severe dengue, often accompanied by bleeding and shock, and require hospitalisation.

The annual economic cost of dengue illness in Asia is estimated at US$2 billion (S$2.7 billion), not including the costs of preventive and vector control efforts.

Unfortunately, the situation is likely to remain grim.

Increased urbanisation, travel and migration, the pressures of globalisation, and global warming are likely to maintain dengue transmission at high levels and continue to result in major outbreaks in affected countries.

In Singapore, dengue is considered "hyperendemic" because all four strains or serotypes circulate all year round. Singapore witnessed large outbreaks of dengue in 2013 and 2014 with 22,170 and 18,338 cases respectively, and, while cases are down this year, continued vigilance and preparedness is clearly needed.

Dengue outbreaks come in cycles and it is difficult to predict when the next one will happen, or if the predominant serotype will change.

The economic burden of dengue in Singapore from 2000 to 2009 is estimated each year to range between US$0.85 billion and US$1.15 billion, of which 41 per cent to 58 per cent is direct medical, direct non-medical and indirect costs such as loss in work productivity, and reduction of household services. The remainder is the cost of vector control efforts.

Dengue control remains both a challenge and an enigma.

In the absence of effective treatment for severe dengue disease, the mainstays of dengue control have been to reduce the mosquito vectors which transmit the virus, and a high level of public awareness and community involvement in the fight against dengue.

While vector control remains a key strategy, it has not always been effective. Singapore spent about half a billion US dollars over the past decade on control programmes and has successfully reduced the Aedes premises index to very low levels, yet it still experiences major outbreaks of dengue.

And despite more than 40 years of research, we continue to wait for an effective vaccine.

Because of all these challenges, it is clear that we need to fight dengue on many fronts through an integrated and inter-sectoral approach, which includes good clinical case management, surveillance with effective field-laboratory-clinic coordination, as well as community participation, engagement and ownership.

Singapore has successfully implemented the Dengue Community Alert System, to alert residents in areas where there is heightened dengue transmission, so that they can take the necessary steps.

But as part of such a strategy we must also continue our search for new and better tools, and to deploy those promising ones which already exist.

First, continued basic research to identify the critical cells in the body which mount a protective immune response to dengue should be pursued, as it may eventually result in novel vaccines. Basic research to develop effective treatments for dengue disease should similarly be a priority. Several leading institutions in Singapore are vigorously pursuing these lines of research. Indeed, one group announced a breakthrough here last week – it had created an artificial antibody that is equally effective against all four serotypes, which is expected to go on human trials next year.

Second, novel methods for suppressing mosquito populations, such as the use of Wolbachia-infected Aedes, should be fully evaluated and tested. Wolbachia is a naturally-occurring bacterium which, when spread among mosquitoes, leads to sterility and reduction in numbers. The National Environment Agency (NEA) of Singapore is evaluating this novel and promising approach.

Third, serious and urgent consideration should be given to deploying the recently-developed dengue vaccine as an important complementary tool in the fight against dengue. Manufactured by Sanofi-Pasteur, the vaccine has completed extensive testing in all phases of clinical trials and has reached the review process by national regulatory authorities for licensing.

Underscoring the importance of the problem, several other vaccine manufacturers also have dengue vaccines which are being evaluated in various phases of testing, and which may become available in the coming years.

At the same time, concerns have been voiced about some of these promising new tools.

Wolbachia-infected Aedes, as a means of controlling the Aedes mosquito, has been tested only in fairly limited pilot studies in Australia, Vietnam and Indonesia, where no adverse effects were observed.

While the results are promising, is the scientific evidence strong enough that it will work in Singapore? Is it safe and how should we assess the safety of an environmental intervention? Is it cost-effective and sustainable in the long term? What is its potential ecological impact on other living things?

Similar concerns have been voiced about the dengue vaccine. Despite extensive testing on 30,000 participants in 10 countries severely affected by dengue, questions have been raised about an inadequate level of efficacy of the vaccine. It offers varying degrees of protection against each of the four serotypes.

For Den-3 and Den-4, it offers 75 per cent protection; for Den-1, it is 50 per cent; and for Den-2, it is 35 per cent, giving an average efficacy of around 60 per cent.

However, the myth that a vaccine needs to be 90 per cent to 100 per cent effective before it is used should be put to rest.

Many vaccines widely used today (to prevent influenza and typhoid fever, for instance) have efficacies ranging from 25 per cent to 70 per cent. While the dengue vaccine in question may not be perfect, emphasis should be placed instead on the finding that it significantly reduced (by 80 per cent to 90 per cent) the incidence of severe dengue disease and the number of hospitalisations.

The cost savings for the population and the healthcare delivery system are likely to be considerable.

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Sophisticated mathematical modelling studies have also indicated that the vaccine will have a significant impact on dengue disease incidence. In the final analysis, however, the rigorous evaluation of the actual impact and effectiveness of any dengue vaccine should be an important part of future implementation programmes.

I believe that we have reached an important crossroads. It is a moral and ethical imperative to act with what we have in hand, be it novel methods to control the vector or an effective vaccine to prevent dengue. Let us seize the moment and use the "third and second best" to deal with the major public health scourge of dengue, and improve the well-being of people in affected countries. In doing so, and in acting now, we should also adopt a "learning by doing" perspective where we strive to learn more about these methods as we deploy them.

While the importance of basic biomedical research to advance fundamental knowledge about dengue is obvious, we need to emphasise that what is already available can make a difference, and should be deployed without delay.

In the words of the Harvard psychologist B. F. Skinner, "the ultimate worth of a science is in how much good it can do in the world".

Dengue control deserves the best tools that science can now offer.

About the author

Professor Tikki Pang, 63, has been a visiting professor at the Lee Kuan Yew School of Public Policy since 2012.

He does research on global health matters and teaches students in the Master of Public Policy and Master of Public Administration programmes.

Last year, he was also appointed chair of the Board of South-east Asia Community Observatory – a community-based research platform between Malaysia and Monash University in Australia which looks at research in the clinical and biomedical sciences, social sciences, economics, education and environmental sciences.

Prof Pang was director of research policy and cooperation at the World Health Organisation (WHO) from 1999 to 2012. He was also co-director of its Collaborating Centre for Dengue and Dengue Haemorrhagic Fever at University of Malaya in Kuala Lumpur from 1982 to 1995, and a member of the WHO Technical Advisory Group on Dengue in 1986.

Based in Singapore and Geneva, Prof Pang holds Bachelor of Science (Honours) and PhD degrees from the Australian National University in Canberra in the fields of biochemistry and microbiology/ immunology.

His main research and academic interests include infectious diseases, global health governance and national health research systems.

In these areas, he has published more than 250 scientific articles and 12 books, edited volumes and reports. These include several major WHO reports, including Genomics And World Health (2002), the World Report On Knowledge For Better Health (2004) and A History Of Research In WHO (2010).