

## The Human Immunodeficiency Virus (HIV) Epidemic in Singapore—Where Are We Now, and Can We “Get to Zero”?

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December 1, 2012 marked the global community's 25th observance of World Acquired Immune Deficiency Syndrome (AIDS) Day. The Joint United Nations Programme on human immunodeficiency virus (HIV)/AIDS (UNAIDS)'s World AIDS Day Report 2012 cited historic gains and laudable achievements towards ending the global AIDS epidemic.<sup>1</sup> HIV incidence fell by 50% in 25 low- and middle-income countries between 2001 and 2011—more than half of these were in sub-Saharan Africa where the majority of new HIV infections occur. In 14 countries, AIDS-related deaths declined by over 50% between 2005 and 2011.

In Singapore, a cumulative total of 5521 HIV-infected residents have been reported as of June 2012.<sup>2</sup> Although Singapore is considered to have a low level HIV epidemic,<sup>3</sup> the annual number of newly diagnosed HIV cases has remained steady at between 440 to 465 cases each year over the last 4 years, with no significant declines seen.<sup>4</sup> Articles in this HIV-themed issue of the *Annals* present important findings and highlight current challenges in the areas of HIV prevention, diagnosis and management.

HIV prevention programmes have shown some success over the past 2 decades. However, many challenges remain. Wong et al<sup>5</sup> discuss several worrying trends in sexual behavioural risk factors among at-risk groups and propose prevention education interventions for the future. Understanding high-risk behaviours among at-risk groups is important for the control of HIV. Community-led initiatives have been a cornerstone of the response to HIV since the beginning of the epidemic. Choong et al<sup>6</sup> describe a local community-based organisation's efforts in adopting a focused, psychosocial approach for men who have sex with men (MSM). Recognising the importance of addressing psychosocial issues to reduce risky sexual behaviours, the organisation combined needs-specific inter-personal skills programmes, community-based psychosocial education approaches, and education on HIV and sexually transmitted infections, so as to holistically improve the psychosocial and sexual well-being of MSM and provide them with the necessary skills for safer sex practices.

The review by Azwa et al<sup>7</sup> tackles another aspect of prevention in which Singapore and other countries have achieved greater success—the prevention of mother-to-child transmission (MTCT). The authors discuss current management strategies of HIV in pregnancy with emphasis on antiretroviral therapy (ART) and obstetric care in a middle income country such as Malaysia. The option of continuing ART for life in all HIV positive pregnant women irrespective of CD4 count has recently been proposed by the World Health Organization (WHO) as a move towards simplification of regimens and service delivery, prevention of MTCT in future pregnancies, and avoiding stopping and restarting ART. This recommendation will greatly expand the number of women eligible for ART globally including Singapore and should give further impetus to efforts towards universal access to ART.

The need for improved and targeted preventive efforts for older patients is highlighted by two articles (Huggan et al<sup>8</sup> and Lee et al<sup>9</sup>). A high proportion of newly diagnosed HIV/AIDS cases in both studies were aged 50 years and above. These older patients presented with lower CD4 counts and more non-AIDS morbidity compared to their younger counterparts. Similarly, Chow et al<sup>10</sup> found that in the period of 1996 to 2000 in Singapore, older patients were more likely to die within 5 years of HIV diagnosis than those under the age of 60. The rapid ageing of the Singapore population combined with risk behaviours amongst older men will continue to shape the local HIV epidemic. Health education for older male patients and effective healthcare planning are needed to reduce the burden of infection and manage its consequences. Going beyond the traditional prevention strategies of abstinence, being faithful to one's partner and condom use, Prof Chan<sup>11</sup> reviews the results of randomised controlled trials studying the use of ART and other biomedical interventions to prevent HIV transmission.

Complementary to preventive services, early testing and linkage to care, as well as appropriate laboratory support are critical in reducing HIV transmission in the community. Verrall et al<sup>12</sup> report on acute retroviral syndrome mimicking dengue, illustrating the potential for misdiagnosis in dengue-

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endemic areas like Singapore if appropriate confirmatory diagnostic tests are not performed. Patients with dengue-like illness may represent a population to be targeted for HIV screening, although studies on the logistics, yield and cost-efficacy of such a strategy in dengue-endemic settings are required. Chew et al<sup>13</sup> compared an in-house Sanger sequencing-based genotype resistance testing method developed at the Communicable Disease Centre (CDC), Singapore, to the US Food and Drug Administration (FDA)-approved ViroSeq™ HIV-1 Genotyping System. The assay successfully identified drug resistance mutations in both subtype AE and B, making it suitable for efficient treatment monitoring in genetically diverse populations. At less than half the running cost of the ViroSeq™ assay, this assay could be a useful addition to the currently limited HIV genotyping assay options for resource-limited settings.

As people living with HIV survive for longer periods on combination antiretroviral therapy (cART), there is increasing awareness of the role of non-AIDS HIV-associated complications. Wong et al's<sup>14</sup> retrospective review of the causes of death in hospitalised HIV-infected patients found that a majority (54.7%) of patients died of non-AIDS defining illnesses. Virologically suppressed patients were more likely to die from non-AIDS defining causes. The presence and persistence of immune dysfunction and chronic inflammation before and after initiation of cART have been linked to end-organ dysfunction and the accelerated expression of non-AIDS morbidity. These phenomena may be exaggerated with age and are thought to explain why cART does not fully restore health or lifespan in older people living with HIV/AIDS (PLHA).

Win et al<sup>15</sup> report on the phasing out of stavudine as a first-line agent, reflecting the change in the WHO guidelines as well as the wider availability of tenofovir in the region. However, a significant minority (18.7%) of their cohort remains on stavudine, underscoring that not all patients are able to access the recommended first-line treatment. For patients on appropriate cART, there are still the pitfalls of unexpected drug-drug interactions including efavirenz which is a component of most first-line regimens (Lee et al)<sup>16</sup> as well as the potential of immune reconstitution inflammatory syndrome (Young et al).<sup>17</sup>

Even as we increase our armamentarium of HIV prevention, diagnostic and treatment tools, HIV-related stigma and discrimination continue to act as potent barriers to effective responses. Fear of stigma and discrimination negatively impact people's will to be tested or to seek medical care, as illustrated by Dr Ng's article.<sup>18</sup> Tackling this issue at all levels of society is thus vitally important.

Singapore has made significant progress in its efforts to fight the HIV epidemic. However, more can, and must, be done. Our success will be measured by our progress towards the lofty goals articulated in the 8th Singapore

AIDS Conference Declaration—“Getting to Zero—Zero Stigma, Zero New Infections, Zero Deaths” from HIV/AIDS in Singapore.<sup>19</sup> Scientific and societal advancements have moved this vision to within the realm of possibility. “Getting to Zero” will require that we continually develop, adapt and apply evidence-based strategies in a sustainable and coordinated fashion. These strategies must be underpinned by strong political will and leadership, concerted multisectoral efforts, community ownership and activism, and continued resolve towards the creation of an enabling environment which empowers people living with HIV to lead dignified lives, as well as strengthens HIV care and prevention efforts.

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