

Essay

「エイズに対する戦いの最前線—治療から予防へ」
[第 16 国際エイズ会議（トロント，カナダ，2006 年 8 月 13-18 日）報告]
“The fights against AIDS shift from Treatment to Prevention” :
[Report of XVI International AIDS Conference
(13-18 August 2006, Toronto, Canada)]

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1996 年のバンクーバー会議が、「エイズ治療（HAART の確立）」の歴史的転換点となったと同様に、くしくもその 10 年後に開催されたトロント会議は、「エイズ制圧に対する戦いの焦点が「治療」から「予防」への大きな転換点」となったということで、後世に記憶されることになるかもしれない。このような転換をもたらした一つの大きな要因は、従来型の公的グラントに加え、特にゲイツ財団などからワクチン開発を含む予防技術開発とその治験に対して巨額且つ組織的な資金援助が始まったためである。本小エッセイでは、このような背景をバックとして、とりわけ疫学的視点からみて、今後のエイズの制圧に向けた研究および対策に重要な影響があると考えられるエイズ世界流行の最新動向と、流行制圧に向けた最新戦略とそのアプローチに関して述べたいと考える。

The XVI International AIDS Conference (IAC, AIDS 2006) in Toronto has attracted record 24,000 participants worldwide, including prominent researchers, policy makers, non-profit organizations, volunteers and students as well as activists. A total of 4,500 abstracts,

both oral and poster, braced with significant new knowledge related to this deadly disease, which have claimed 38.6 million infections worldwide, have been presented in this 1-week meeting. Major tracks in this conference encompassed basic and clinical sciences,

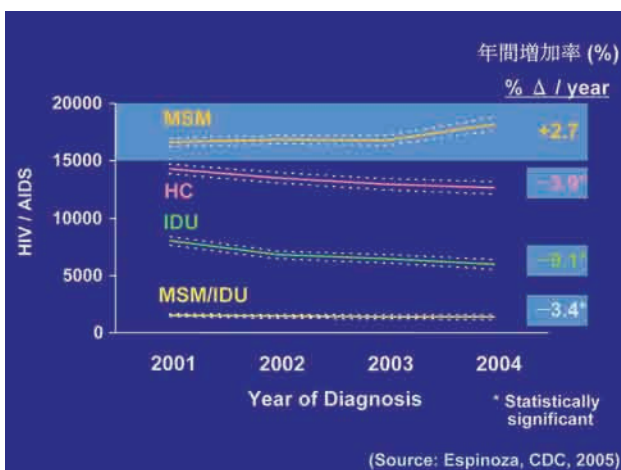


Figure 1 Estimated Number of HIV/AIDS Diagnoses, by Transmission Category, 2001-04. MSM 間での HIV/AIDS 流行の再興（リエマージェンス）（米国，2001-04）（Espinoza, CDC, 2005）

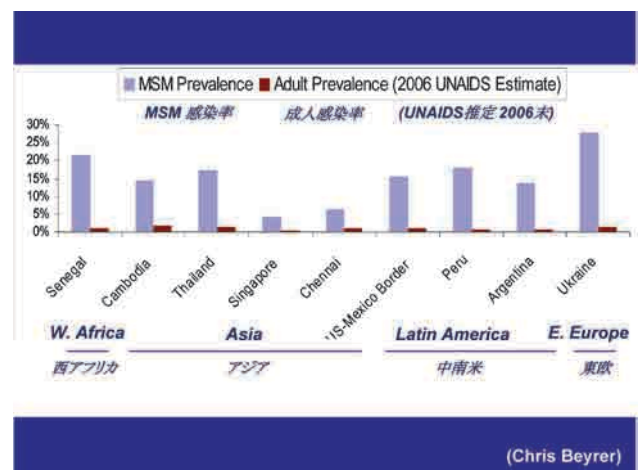


Figure 2 Global trend : Emergence and reemergence of HIV epidemic among MSM. 世界規模で MSM 間の HIV/AIDS 新興・再興流行が起こっている（Chris Beyrer）

epidemiology, prevention, socioeconomic and behavioural sciences, and policy scope.

As we discuss later, this meeting will be recollected in future as a critical turning point of shifting the priority research agenda from treatment to prevention, putting much emphasis on multi-facet development of novel prevention technologies through concerted international collaborations. In this short commentary, we will discuss on the new trends of HIV/AIDS research and development as well as selected topics of our interests.

Global epidemiology of HIV/AIDS : new trends in HIV pandemic

Chris Beyrer from John Hopkins Bloomberg has kick-off the conference with a comprehensive plenary lecture on HIV epidemiology update and transmission factors (MOPL02). In this review, three major themes were discussed in details : 1) injecting drug user (IDU) through Eurasia, 2) trends among men who have sex with men (MSM) in high and low income countries, and 3) the epidemic in South Africa.

1) Emerging epidemics in Eurasia driven by IDU : The Russian Federation and Ukraine have reported the highest increase in HIV cases between 1987 and 2005 and several structure drivers of spread across Eurasia have been determined, including the close geographic proximity to overland drug trafficking routes (e.g., the Middle East), limited use of HIV prevention measures with demonstrated efficacy for IDU transmission and punitive and legalistic approaches to IDUs.

2) New trends of epidemics among MSM : The trends among MSM, meanwhile, have witnessed a significant increase in HIV incidence over the last two years compared to other transmission risks in the United States. African American MSM in the US are also reported to be more 'susceptible' to HIV infection probably due to lack of socioeconomic privileges (see also THBS0202 by Stall *et al*) (Fig. 1). Interestingly, a sharp increase of HIV incidence among MSM in Thailand and Cambodia is also highlighted^a (Fig. 2).

3) Southern African epidemics : The South African epidemic have accentuated several determinants for sexual transmission of HIV in the region : lack of condom use, level of blood viral load, genital viral load, lack of circumcision, genital ulcerations and inflammatory STDs plus lack of access to antiretroviral therapy.

New insights into biological significance of HIV-1 recombination

In the domain of basic sciences, 1) a study by Arts

^aTreatAsia Special Report : "MSM and HIV/AIDS Risk in Asia : What is fueling the epidemic among MSM and how can it be stopped" (August 2006)

et al (TUAA0204) has demonstrated that infection with HIV-1 subtype C of lower replicative fitness as compared to subtypes A and D leads to slower disease progression in Zimbabwean and Ugandan women. Previous studies by the author revealed that subtype C, which responsible for 60% of infections worldwide, are at least 100-fold less fit than any HIV-1 isolates from group M. In this present study, the rate of disease progression of Zimbabwean infected with subtype C was compared to that of Ugandan infected with subtypes A or D. By measuring the CD4 cell decline for over 2 years of follow-up, the Ugandan patients showed a significantly faster decline than the Zimbabwean and these differences appeared to be related to HIV-1 subtypes. Upon extrapolation, Ugandan patients were estimated to have progressed to AIDS in 8 years compared to the Zimbabwean patients of 20 years. The authors concluded that when compared to subtype A and D, reduced replicative fitness of subtype C may be linked to slower disease progression. Similarly, several studies are also focusing on the ex-vivo viral fitness of different HIV-1 subtypes/circulating recombinant forms (CRFs). 2) For instance, Rubio *et al* (WEPE 0006) from Argentina found that although subtype F has a higher replicative fitness than subtype B, the recombination event between these subtypes did not increase the replicative capacity of the BF recombinant in peripheral blood mononuclear cells. These results further emphasized low fitness of the subtype C, which is now beginning to circulate in Argentina. 3) In clinical settings, effect of HIV-1 recombinant subtypes on disease progression in European seroconverter cohorts was also presented (TUPE0018). Non-B subtypes, particularly recombinants, have been introduced in European cohorts and their frequency has increased over time. Among antiretroviral-naive patients infected with recombinant subtypes other than CRF02_AG, the authors revealed that CD4 counts are lower than in those with B subtype.

Emergence of novel HIV-1 recombinants

In a narrower scope of HIV-1 molecular evolution, Tovanabutra *et al* has described the link between multiple HIV-1 exposure and genetic complexity of strains that is reinforced by identification of a second CRF among IDUs in northern Thailand (TUAA0201). In this molecular epidemiological study, two new CRFs (CRF15_01B and CRF34_01B) and many unique recombinant forms of HIV-1 have been identified among IDUs in Thailand, confirming that IDU risks contribute to the genetic complexity of the epidemic. The authors concluded that comprehensive prevention services for IDUs and other highly exposed risk groups could help to limit the growing complexity of HIV-1 strains in

Thailand. Similarly, our study in Malaysia (WEPE0020) also uncovered a novel CRF (CRF33_01B) plus various unique recombinant forms in a majority-IDUs HIV epidemic in this country. So far, a total of 34 CRFs have been currently recognized (<http://hiv-web.lanl.gov/CRFs/CRFs.html>) (CRF34_01B from Thailand is the newest addition in this category). Taken together, these investigations have underscored the multifaceted genetic diversities of HIV-1 in the Southeast Asia region that may add more burdens for future clinical trials involving therapeutic or prophylactic candidate vaccines.

Shifting priority from treatment to prevention : New Approaches to HIV Prevention^b

Twenty-five years into the global HIV/AIDS epidemic, HIV infection rates are alarmingly high, more than 4 million people become infected and 3 million people died of AIDS every year. Despite the successful introduction of 3 by 5 programme by WHO/UNAIDS initiative, only limited fraction of the people have access to the treatment.

An exhilarating plenary lecture by Gita Ramjee (TUPL02) has highlighted several promising areas of effective HIV prevention (Fig. 3). In addition to Bush's administration's infamous **A (Abstinence)**, **B (Be Faithful)** and **C (Condom or Counselling & Testing)**, she reviewed new prevention strategies (**D** through **I**) (Fig. 3) and priority research agenda that are now

^bGlobal HIV Prevention Working Group (Executive Summary) : "New Approaches to HIV Prevention : Accelerating research and ensuring future access" (August 2006). (also see www.gatesfoundation.org, www.kff.org and www.care.org)

richly sponsored by the international philanthropic organizations, including the Bill & Melinda Gates Foundation.

- 1) "**C (Male Circumcision)**" : Novel male-initiated prevention strategy of circumcision has received positive attentions as seen in several ethically-challenged efficacy trials recently.
- 2) "**D (Female Diaphragm)**" : The use of female diaphragm and cervical barrier to prevent HIV and other sexually transmitted infections (STIs) has also been highlighted, giving more power to woman to uphold their rights to protect themselves.
- 3) "**E (Pre- and Post Exposure Prophylaxis with Anti-retrovirals)**" : Interventions by pre- and post-exposure prophylaxis have taken a step forward based on the success of antiretroviral therapy including tenofovir and truvada in clinical settings. The safe and simple drug regimen has given these drugs the added values to be enrolled in several efficacy trials.
- 4) "**F (Female-Controlled Microbicides)**" : A number of candidate microbicides (virucidal compounds that are applied in vagina to prevent HIV acquisition) have been enrolled in phaseIIb/III trials and provide some early indications that this female-initiated approach could be a fruitful effort in controlling HIV spread. Further evidence-based results are pending.
- 5) "**G (Genital Tract Infection Control)**" and "**H (HSV-2 Suppressive Treatment)**" : The coexistence of herpes simplex virus 2 (HSV-2) has been associated with increased HIV-1 transmission and acquisition risks. Thus by suppressing HSV-2, the transmission cycle of HIV would be disrupted and at the meantime reducing the disease morbidity in the patients.

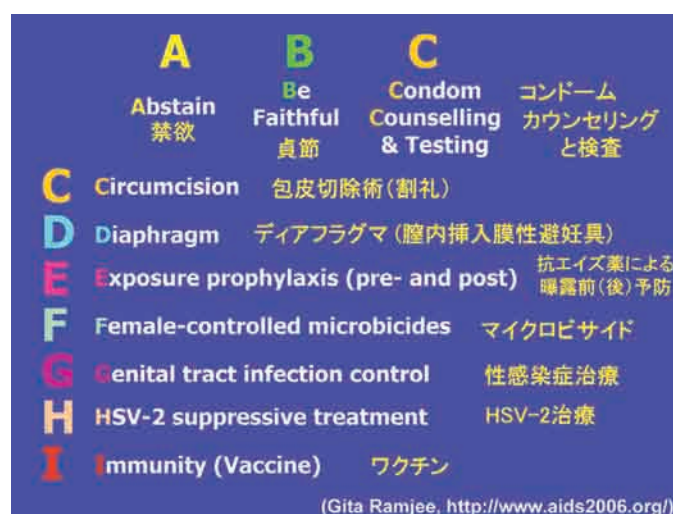


Figure 3 New approaches to HIV prevention. HIV 感染予防に向けた新しいアプローチ (Gita Ramjee, from the official web site for XVI International AIDS Conference, <http://www.aids2006.org/>) (modified)

6) "I (Immunity (Vaccine))" : Lastly, the pursuit for an effective vaccine has always been the ultimate prevention of HIV worldwide. Several major areas including the study of the host innate immunity against HIV infection has been identified and prioritizing such areas would be the backbone in developing prophylactic or therapeutic vaccine candidates with promising public health impact.

We hope that these concerted efforts in global scale will effectively combat and control HIV/AIDS, the unprecedented human sufferings, in the world.

Acknowledgements

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