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Challenges and counter challenges in HIV/AIDS

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Editorial

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Since the beginning of the HIV/AIDS pandemic, there has been significant progress in combating the virus. In addition to identifying HIV,[1] scientists have developed an array of antiretroviral drugs and successfully converted the once deadly disease into a treatable and chronic condition.[2] Nevertheless, this battle is far from over and HIV still outsmarts humans in multiple ways and poses tremendous challenges. Within this context, the *Chinese Medical Journal* has timely published this special issue on HIV/AIDS, highlighting the ongoing challenges posed by HIV and potential solutions to these problems.

The most daunting challenge is to develop prophylactic measures such as vaccines and microbicides to prevent HIV transmission. HIV vaccine development has been dominated by a theme of frustration and failure, best exemplified by the futility of the Merck Ad5 phase IIb T-cell vaccine.[3] Recently for the first time in the history of HIV vaccine efficacy trials, human RV144 Thai trial revealed a modest but significant improvement in efficacy against HIV transmission.[4] However, researchers still have yet to identify the immune correlates of RV144-vaccine-induced-protection or to find the best way to design HIV vaccine post-RV144 to enhance modest protection to a level that is practical for clinical use. Recent reconstruction of an exceptionally broadly neutralizing antibody-VRC01[5,6] using novel approaches may open a new avenue for better understanding and design of immunogenic antigen to elicit broadly neutralizing antibodies through vaccination.

Dr. Wan and colleagues[7] on page 3489 of this issue reviewed the current state of HIV-1 vaccine development encompassing the present understanding of the basic biology of newly transmitted virus, tailoring innate immune response through toll-like receptors and dendritic cells to elicit protective adaptive immunity, especially at the mucosal site of viral entry. Of note, this review also covered the important issues of immunogenicity, new adjuvants and replication competent vectors, and the state of AIDS vaccine clinical trials in China.

Similar to the difficulties in developing an HIV vaccine, HIV microbicides have also faced numerous unsuccessful efficacy trials except for the recent CAPRISA 004 trial. The 004 trial demonstrated a reduction of HIV acquisition by an estimated 39% overall and by 54% in women with high gel adherence using 1% vaginal gel formulation of tenofovir, a nucleotide reverse transcriptase inhibitor.[8] Many of topical microbicide candidates advanced into clinical trials have failed, such as nonooxynol-9, because they can cause mucosal inflammation and damage.[9] Thus identification of mucosal inflammatory biomarkers to evaluate the mucosal toxicity of candidate microbicides is urgently needed. Dr. Li and his colleagues[10] on page 3381 assessed the cytokine profiles in mouse vaginal secretion and histopathological changes in cervicovaginal mucosa after vaginal exposure to Nonooxynol-9. They found that interleukin-17A (IL-17A), IL-6, IL-4 and IL-10 are significantly correlated with mucosal damage caused by nonooxynol-9. This study indicates that profiling of cytokines in vaginal secretion may be a useful tool to predict the mucosal toxicity induced by candidate microbicides.

Some other challenges in the HIV/AIDS research field are treatment related, such as drug resistance, complications associated with anti-retroviral therapy (ART), and treatment management in persons with opportunistic infections or other pathogen coinfection.

HIV drug resistance can be acquired through transmission and/or post transmission during ART, jeopardizing the success of ART. Detecting and monitoring of drug-resistant virus is of importance for treatment management at individual and population levels.[11] Since developing countries use different and limited ART drugs from developed countries, drug resistance data from foreign registries are not directly applicable.

Dr. Guo and his colleagues[12] on page 3389 reported the detection of the most common non-nucleoside reverse transcriptase inhibitor (NNRTI) or nucleoside reverse transcriptase inhibitor (NRTI) drug resistant mutations in Chinese HIV^+ individuals using allele-specific real-time PCR and found this method to be much more sensitive than bulk sequencing. This method can now be used to monitor drug resistance in HIV infected individuals in China.

Dr. Zeng and his colleagues[13] on page 3396 in this issue measured arterial stiffness using pulse wave velocity (PWV) analyses in Chinese HIV^+ individuals. They found

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that HIV^+ individuals not receiving ART have significantly higher PWV than that of HIV^- individuals, indicating that HIV infection may increase arterial wall stiffness; HIV^+ individuals receiving ART (only NNRTI or NRTI) have significantly lower PWV than that of HIV^+ individuals not receiving ART.

Dr. Zhang and his colleagues[14] on page 3400 conducted a retrospective cross-sectional study on pulmonary tuberculosis in HIV^+ individuals and found that 4.4% of Chinese HIV^+ individuals (CD^+ <350 cells/μl) were coinfected with pulmonary tuberculosis.

While the conclusions of the above three studies need to be validated in a more powered and longitudinal studies, the results of these studies are informative.

HIV R144 vaccine trial provides us optimism for countering the challenges posed by HIV/AIDS; nonetheless there is still a long fight ahead against this versatile virus. This special issue on HIV/AIDS is just another step of this long journey to the ultimate defeat of HIV.

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