

AIDS is not over

IWAMOTO Aikichi^{1*}, LIU HuanLiang² & LI Hong³

¹Institute of Medical Science, The University of Tokyo, Tokyo 108-8639, Japan;

²Institute of Human Virology and Key Laboratory of Tropical Disease Control of Ministry of Education; Guangdong Institute of Gastroenterology and the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou 510655, China;

³Yunnan Center for Disease Control and Prevention, Kunming 650022, China

Received January 13, 2015; accepted March 9, 2015; published online March 24, 2015

Citation: Iwamoto A, Liu HL, Li H. AIDS is not over. *Sci China Life Sci*, 2015, 58: 517–518, doi: 10.1007/s11427-015-4840-5

Acquired immunodeficiency syndrome (AIDS) was first reported in 1981 [1]. Five healthy young men suddenly presented with opportunistic pneumonia caused by *Pneumocystis carinii* (currently termed *P. jirovecii*). The original report from Los Angeles was followed by many reports of patients with similar symptoms in large cities in North America and in Europe. People in resource-rich countries were shocked by this sudden emergence of a highly fatal disease among gay men. Two years later, a brand new retrovirus was isolated [2]. The virus turned out to be the causal agent of AIDS and was named as the human immunodeficiency virus (HIV). The typical natural course of an HIV infection is characterized by three major phases, i.e., acute phase, chronic asymptomatic phase and AIDS phase with severe immunodeficiency. In the acute phase, about half of the patients present with an acute viral syndrome (fever, skin rash, lymphadenopathy, etc.) a few weeks after the infection. The other half may stay asymptomatic. Patients shift from acute to chronic asymptomatic phase a few months following the initial infection. Although the chronic asymptomatic phase lasts for 8 to 10 years on average, the disease progression varies greatly from individual to individual. AIDS is the terminal phase of an HIV infection and characterized with the prevalence of opportunistic diseases.

HIV resides in body fluids, including blood, seminal fluid, and vaginal fluid. Sexual intercourse, and intravenous drug use are the main transmission routes. Mother-to-child transmission also occurs. HIV tends to spread among mi-

norities such as intravenous drug users, female commercial sex workers, and men who have sex with men (MSM). According to the estimation at the end of 2013 by World Health Organization (WHO), around 78 million people globally have become infected with HIV since the start of the epidemic and 39 million died of AIDS-related illnesses. Thirty-five million people were living with HIV/AIDS in 2013: 24.7 million (70%) in Sub-Saharan Africa and 4.8 million (14%) in Asia.

In Asia, the first outbreak of HIV occurred in countries such as Thailand, Cambodia and Myanmar in late 1980s. Bordering Myanmar, Lao and Vietnam, the first cluster of 146 cases in Yunnan province was reported in 1989 from Ruili, a beautiful city at the west corner of Dehong prefecture facing Myanmar. By 2006, 48,951 cases were reported in Yunnan [3]. Circulating Recombinant Forms (CRFs) between subtype B and C HIVs were prevailing in the epidemic. Subtype B had been circulating among drug users in Northern Thailand, while subtype C had spread from Southern Africa to India and Myanmar. The recombination of the two HIV subtypes could have occurred in Yunnan. Following the economic expansion of China, the virus spread from Yunnan to coastal provinces such as Guangxi, Guangdong and even to Taiwan in 2004. The virus spread also to inland provinces such as Xinjiang and Sichuan [3]. Owing to the countermeasures at the country, province, prefecture and county levels, annual reported case numbers in Yunnan have leveled off, however the epidemic is still growing across the country. The province reporting the highest number of HIV infection changed over from Yun-

*Corresponding author (email: aikichi@ra3.so-net.ne.jp)

nan to Guangxi in 2011. From 1989 to 2014, 102,510 HIV/AIDS cases have been reported cumulatively in Yunnan where the disease burden is still the highest in China. Forty-five percent of HIV cases reported in China by the end of 2014 were from Yunnan, Guangxi and Sichuan.

Along with the economic expansion, HIV transmission routes are becoming more diverse and complex in China. Traditionally, intravenous drug use in Yunnan and plasma donation in Henan and surrounding provinces were main transmission routes in China [4]. However, transmission through commercial sex workers and homosexual activity has been contributed more to the expansion of the epidemic. In Yunnan, the most frequent transmission route switched from intravenous drug use to sexual intercourse around 2006. In 2013, sexual intercourse was reported to be the route of transmission in 86% of 10,553 cases.

The drug development for HIV started soon after the discovery of the virus. The first effective drug, zidovudine (AZT), a nucleoside reverse transcriptase inhibitor (NRTI) was approved for clinical use to treat HIV infected patients in 1987. Development of other NRTIs such as didanosine (ddI), zalcitabine (ddC), stavudine (d4T), lamivudine (3TC) followed by the early 1990s. Protease inhibitors such as saquinavir, ritonavir, indinavir, and nonnucleoside reverse transcriptase inhibitor (NNRTI), nevirapine, were approved in the mid-1990s. Combination anti-retroviral therapy (cART) combining three active drugs became available around 1995–1996 in the resource-rich countries. In the early days of cART, patients had to take many pills in a day with dietary restrictions and suffered from many adverse events, but new drug discoveries and the invention of fixed dose combos (two or more active drugs in a single tablet) have made cART safe and simple in resource-rich countries. Furthermore, newer classes of antiretroviral drugs such as integrase inhibitors and fusion inhibitors have been approved and used in clinical practice.

Effective cART was also proven to be very important for HIV prevention [5]. Although China's National Free Antiretroviral Treatment Program started in 2002, much improvement is still needed [6].

As noted above, HIV infection tends to spread in large cities irrespective of the economic state of the country, presumably because of the large population, anonymity, etc. Yunnan is a vast but less densely populated province with many small villages located on the hills and mountains. It is

hard to imagine a heavy HIV epidemic while you are driving in the province. This geography may contribute to the distribution of HIV, which occurs in a scattered manner. Higher numbers have been reported from prefectures on the highways radiating from Kunming such as Dehong (Ruili, Yingjiang), Honghe (Kaiyuan, Hekou) and Lincang (Cangyuan, Gengma). Scattered epidemics are there also in small villages. Cangyuan and Gengma have reported the highest prevalence in Lincang prefecture. In two administration villages there, the recent HIV prevalence was recorded at about 4% of the population.

Many small villages are located far away from the modern medical facilities. HIV-positive villagers need to travel a long way to obtain a physical examination and cART. It would be hard for them to be adherent to treatment even if the government provided free cART. Hence, HIV prevention should be imperative. Scientific research on the spread of this virus should be a necessary component in measures taken to better understand and cope with these newly emerging HIV epidemics in these small villages. Molecular virology research would provide crucial information needed for developing the best prevention.

- 1 Gottlieb MS, Schroff R, Schanker HM, Weisman JD, Fan PT, Wolf RA, Saxon A. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. *N Engl J Med*, 1981, 305: 1425–1431
- 2 Barre-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruest J, Dautquet C, Axler-Blin C, Vézinet-Brun F, Rouzioux C, Rozenbaum W, Montagnier L. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science*, 1983, 220: 868–871
- 3 Lu L, Jia M, Ma Y, Yang L, Chen Z, Ho DD, Jiang Y, Zhang L. The changing face of HIV in China. *Nature*, 2008, 455: 609–611
- 4 Wu Z, Sullivan SG, Wang Y, Rotheram-Borus MJ, Detels R. Evolution of China's response to HIV/AIDS. *Lancet*, 2007, 369: 679–690
- 5 Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Wang L, Makhema J, Mills LA, de Bruyn G, Sanne I, Eron J, Gallant J, Havlir D, Swindells S, Ribaldo H, Elharrar V, Burns D, Taha TE, Nielsen-Saines K, Celentano D, Essex M, Fleming TR; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*, 2011, 365: 493–505
- 6 Zhang F, Dou Z, Ma Y, Zhao Y, Liu Z, Bulterys M, Chen RY. Five-year outcomes of the China National Free Antiretroviral Treatment Program. *Ann Intern Med*, 2009, 151: 241–251, W–52