

HIV/AIDS in Taiwan

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HISTORY AND CURRENT STATUS OF INFECTIOUS DISEASES IN TAIWAN

Taiwan is located in the middle of East Asia. Since Taiwan is a frontier island, it experienced a complicated transformation in ethnicity during the 17th, 18th, and 19th centuries. Taiwan had been occupied by both the Dutch and Japanese. The main population of Taiwan now includes descendants from four ethnic groups: aborigines, Fukienese, Hakka, and mainland Chinese. The native aborigines consist of nine different tribes. The Fukienese and Hakka are early settlers who immigrated from Fukien and Guangdong provinces of China several hundred years ago. The mainland Chinese are people who came to Taiwan from the mainland after World War II. In the past few years, due to a new openness in society following the relaxation of regulations, many immigrants from mainland China and southeastern Asia have come to Taiwan through marriage arrangements. At present, Taiwan's population is about 23 million.

Tuberculosis

As shown in Table 1, several important infectious diseases in Taiwan have been eradicated or have been under control since 1948. Every five years since 1957, the Department of Health (DOH) of Taiwan has conducted a survey on pulmonary tuberculosis (TB). The surveys showed that in 1957, 5.15% of persons aged >20 had pulmonary TB, among them, 20% had infectious TB. By 1993, the rates of pulmonary TB and infectious TB had decreased to 0.65% and 0.06%. Currently, there are about 15,000 new TB cases every year in Taiwan (Center for Disease Control, Taiwan, 2003a). It is worth noting that the incidence of TB in the aborigines in 1998, 239/100,000, was much higher than that in other populations.

Hand-Foot-and-Mouth Disease

In 1998, an epidemic of enterovirus 71 infection caused hand-foot-and-mouth disease (characterized by vesicular lesions on the hands, feet, and oral mucosa) and herpangina

TABLE 1. The Chronicle of the Control of Infectious Diseases in Taiwan

Year	Event
1948	Eradication of plague
1948	Initiation of vaccination program
1955	Eradication of small pox
1959	Eradication of rabies
1965	Eradication of malaria
1984	Initiation of HBV vaccination program
1990	AIDS control law was launched
1995	Initiation of HAV vaccination program
1997	Free HAART was provided
1998	Initiation of influenza vaccination program, especially among elders
1998	Eradication of poliomyelitis was recognized
1999	Infectious disease control law was launched
1999	Establishment of Taiwan CDC by merging three governmental organizations
2001	Formation of AIDS Advisory Committee at the Executive Yuan

in thousands of people in Taiwan, some of whom died. The sentinel physicians reported nearly 130,000 cases of hand-foot-and-mouth disease or herpangina in two waves of the epidemic, which probably represents less than 10% of the estimated total number of cases. There were 405 (0.3% of the total) patients with severe disease. Most of them were five years old or younger, and most of those who died were young. The majority died of pulmonary edema and pulmonary hemorrhage. Enterovirus 71 infection was associated with most of the serious cases and with nearly all the deaths. A laboratory-network was established linking 10 hospitals island-wide together with the Center for Disease Control (CDC) of Taiwan for laboratory diagnosis. This network has been active since then and more laboratories were added to the network when severe acute respiratory syndrome (SARS) attacked Taiwan in 2003 (Ho *et al.*, 1999).

Severe Acute Respiratory Syndrome (SARS)

The outbreak of SARS, originally referred to as atypical pneumonia, was first

identified in Guangdong Province, China in November 2002. By August 7, 2003, SARS had spread to more than 30 countries, affected 8422 people and resulted in 916 deaths worldwide (World Health Organization, 2003). In Taiwan, the first SARS case was diagnosed on March 14, 2003. This index case had traveled to Guangdong, China in February. On April 24, the Taipei city government announced that it was closing down Ho-Ping Hospital for two weeks. Although the government imposed mandatory 14-day quarantine on all air travelers from China, Hong Kong, Singapore, Macau, and Toronto on April 28, the SARS epidemic spread in Taiwan island-wide and more than 29 hospitals reported nosocomial infection. According to the Center for Disease Control of Taiwan, of the 664 probable SARS cases reported to the World Health Organization, there were 346 SARS cases confirmed by either RT-PCR or serological test (Figure 1) (Center for Disease Control, Taiwan, 2003b).

HISTORY AND CURRENT STATUS OF HIV-1 INFECTION IN TAIWAN

The first indigenous AIDS case in Taiwan was found in 1986, and as of Oct 2003, 5464 people living with HIV-1 (hereafter referred to simply as HIV) and AIDS (PLWHA) had been reported to the Department of Health of Taiwan. This number included 5042 Taiwan citizens and 422 foreigners. The numbers of PLWHA increased rapidly, with a rate of increase of more than 15% every year (Figure 2). The male-to-female ratio of the reported cases was 13 to 1. According to risk factor analysis, 40.6% of the cases were heterosexuals, 36.5% were men who have sex with men (MSM), 12.2% were bisexuals, 2.0% were intravenous drug users (IDU), and 0.24% were infected by blood transfusion; 53 cases were among hemophiliacs, and nine cases were due to vertical transmission (Center for Disease Control, Taiwan, 2003c). It has been speculated that the true number

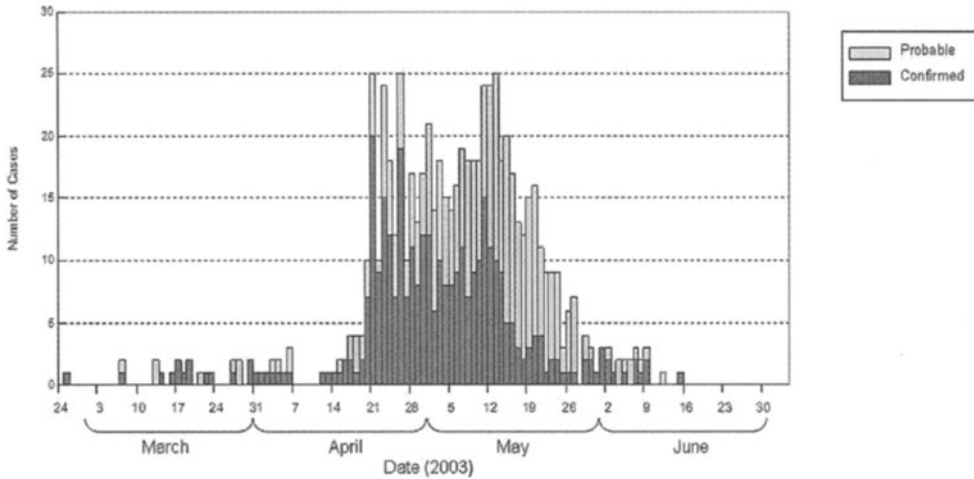


FIGURE 1. Epidemiological curve of the probable and confirmed SARS cases in Taiwan. The confirmed cases were proved by either RT-PCR or serological test. (CDC Taiwan, 2003b)

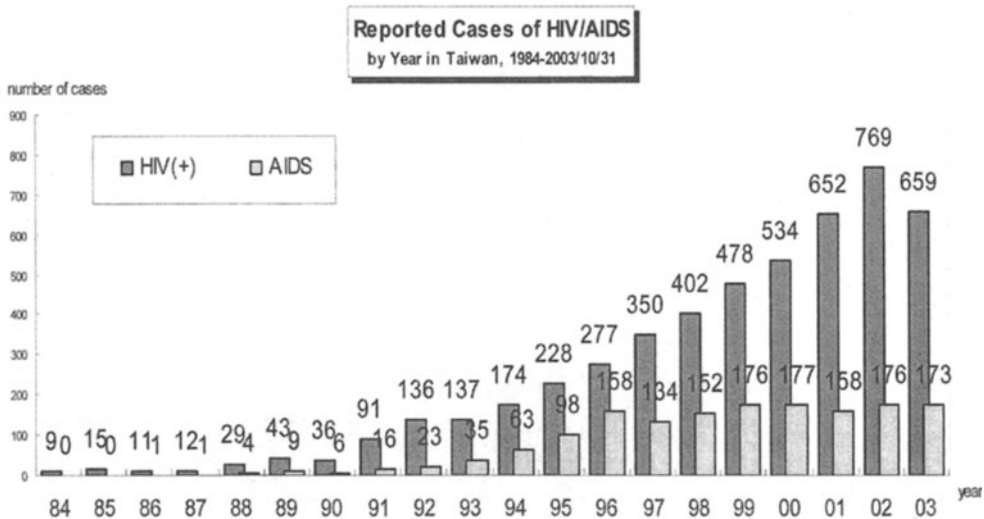


FIGURE 2. The cumulative numbers of HIV/AIDS cases reported to CDC of Taiwan by the end of October 2003. (CDC Taiwan, 2003c)

of PLWHA in Taiwan is about 2–3 times the reported cases.

There are several important characteristics of the HIV/AIDS epidemic in Taiwan: more than 80% of infections have been due to sexual transmission, less than 2% of infections have been as a result of needle sharing, and mother-infant transmission has been

very rare. When the trends over time on the distribution of different age groups in the HIV/AIDS patient cohort were analyzed, the results showed that the percentage of patients aged 19 or younger increased from 2% in 1995–1996 to 6% in 1997–1998. In addition, since 1997–1998, the number of patients in their 20s has surpassed the number of those

TABLE 2. The Prevalence Rates of HIV Infection among Different Groups in Taiwan, 2001.

Group	Prevalence Rate
Conscripts	5.3/100,000
First-time blood donors	6.3/100,000
Pregnant women	14.5/100,000
IDU	89.7/100,000
Prisoners	112.0/100,000
FSW ^a	200.0/100,000
STI patients	1,900.0/100,000
MSM in gay saunas	6,700.0/100,000

^a 1996 data.

in their 30s and has become the largest age group (Chen *et al.*, 2001b). This is an alarming sign that HIV/AIDS education among Taiwan's youth needs to be strengthened.

The Prevalence of HIV Infection in Different Groups in Taiwan

Men Who Have Sex with Men

As shown in Table 2, judging by the HIV prevalence rates in the populations of conscripts, first-time blood donors, and pregnant women, the general public in Taiwan had a lower rate of HIV infection than other countries in Asia (Monitoring the AIDS Pandemic Network, 2001). Among different high-risk groups in Taiwan, MSM in gay saunas had the highest rate of HIV infection. According to our surveys, the rates of HIV-1 infections among MSM in gay saunas in different cities were: 15.8% (22/139) in Kaohsiung in 1999, 9.5% (33/348) in Taipei in 2000, 5.2% (16/307) in Taipei in 2001, and 6% (6/100) in Taichung in 2002. Besides HIV, this population also had quite high rates of syphilis infection, ranging from 8.1 to 13.8% (Center for Disease Control, Taiwan, 2003c).

Sexually Transmitted Infections (STI)

Both the male homosexual and bisexual HIV/AIDS patients had significantly higher

rates of syphilis infection than the heterosexual men in Taiwan. In contrast to the high rate of sexual contact with sex workers in the male heterosexual subgroup, only 16.6% of the HIV-positive MSM had sexual contact with sex workers (Chen *et al.*, 1998a; Chen *et al.*, 2001b). Therefore, the high rate of syphilis infection among HIV-positive MSM may reflect the prevalence rate of syphilis infection in the MSM population in Taiwan. In Taiwan, the HIV-positive MSM were much younger than the HIV-positive heterosexual men were. According to the Yang-Ming AIDS Center database, about 55% of the HIV-positive MSM were aged below 30, while about 30% of HIV-positive heterosexual men were aged below 30 (Chen *et al.*, 2001b). In addition, the group of MSM patients had a higher percentage of persons aged below 20 than the heterosexual group, 3.0% vs. 1.7% (Chen *et al.*, 2001b). This suggests that MSM might be engaging in high-risk behaviors at a younger age than heterosexual men in Taiwan. The synergistic relationship between HIV and certain STIs, especially genital ulcerative diseases, has been reported previously (Plummer, 1998). The lack of sex education and the existing stigmatization of homosexuality both considerably increase the risk for MSM of contracting HIV and other STIs in Taiwan. Therefore, it is important to develop an effective HIV and STI prevention program targeting MSM in Taiwan.

Heterosexual Population and HIV Subtypes

Changes over time in the distribution of different HIV subtypes in the heterosexual population are very striking. According to our analysis, more than half of heterosexual males had HIV subtype B infection, but CRF01_AE surpassed subtype B and became the major subtype between 1997 and 1998 (Figure 3) (Chen *et al.*, 2001b).

According to risk factor analysis, nearly half of the HIV-positive heterosexual males admitted that they had sexual contact with sex workers when they went to Southeast Asia.

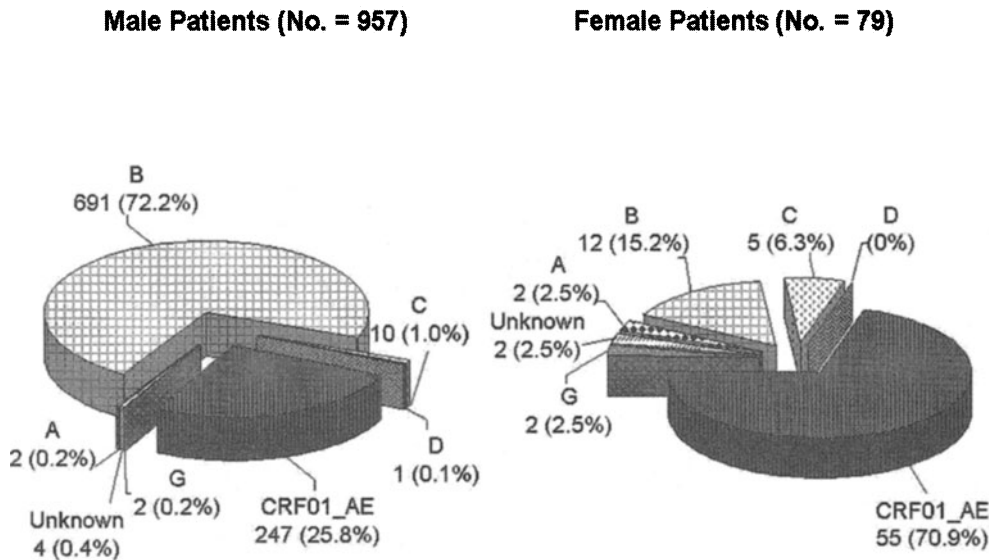


FIGURE 3. Proportions of HIV-1 subtypes in the male and female HIV/AIDS patients recruited by the Yang-Ming AIDS Center from 1988 to 2000 in Taiwan.

This is consistent with the results of the phylogenetic analysis which showed that most of the Taiwanese CRF01_AE clustered with isolates from Thailand (Figure 4).

Women with HIV/AIDS

As shown in Figure 3, about 85% of the female HIV/AIDS patients were infected with non-B clades, with CRF01_AE as the predominant subtype. In Taiwan, the most important risk factor for women was that their husbands were seropositive. Previously, we have reported the results of a study that found 17 of 52 (32.7%) married couples were seroconcordant. When the HIV subtypes of the couples were analyzed, 14 of 33 (42.4%) husbands infected with CRF01_AE had transmitted HIV to their wives, while only 1 of 17 (5.9%) men with subtype B had transmitted the disease to their spouses ($p < 0.01$). Both of the two husbands infected with subtype C had also transmitted HIV to their wives (Chen *et al.*, 2001b). Other recent studies in Thailand have also shown subtype differences, both in level of viral replication during seroconversion and in transmissibility in cohorts of IDU

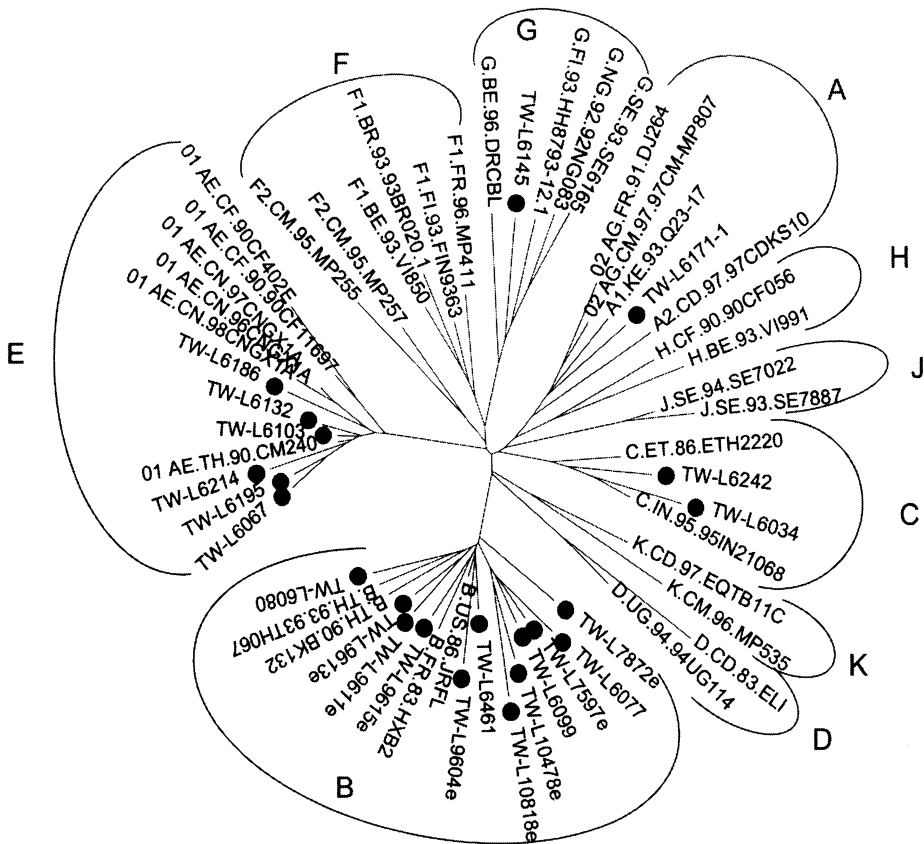
(Hu *et al.*, 2001; Hudgens *et al.*, 2002). Studies on the virological characteristics of both HIV subtype C and CRF01_AE have revealed that they may have adapted better to transmission through the human population (Ping *et al.*, 1999; Montano *et al.*, 1998).

Female Sex Workers (FSW)

In Taiwan, most FSW are infected with HIV CRF01_AE (Chen *et al.*, 2001b). There is a risk of an increasing spread of HIV E in the heterosexual population in Taiwan. In a survey of HIV and STI prevalence among FSW in the Taipei metropolitan area from 1993 to 1996, 0.2% (2/1036) of FSW from karaoke bars were found to have HIV, while none of the 725 FSW from massage parlors and 484 FSW from brothels were infected with HIV (Chen *et al.*, 1998b). Due to the lack of subsequent follow-up study, the current prevalence of HIV infection in this population is unknown.

Injecting Drug Users (IDU)

The prevalence of HIV infection among Taiwanese IDU has never been reported.



Phylogenetic Tree Analysis of HIV-1 Isolates from Taiwan

FIGURE 4. Phylogenetic analysis of Taiwanese (TW-) HIV-1 isolates. The neighbor-joining tree was obtained from 100 bootstrap samples of aligned *env* sequences corresponding to the nucleotide residues 7062–7379 of HXB2 from different HIV-1 isolates.

There is relatively little control of the medical supplies market in Taiwan, and syringes are easy to obtain. Because of this, there appears to be a much lower rate of needle-sharing in Taiwan, with the possible exception of the prison inmate population. Although less than 2% of the total number of reported cases of HIV/AIDS were among IDU, it is important to note that according to a survey conducted by a social worker visiting prisons island-wide, the numbers of HIV-positive inmates tripled between 2001 and 2003 (Sr. Teresa Hsieh, Director, Lourdes Home of Taiwan, personal communication, October, 2003). In terms of subtypes, according to our previous study on 22 IDU, 12 heterosexual men and one MSM were infected with HIV B subtype, six heterosexual

men and one MSM were infected with HIV CRF01_AE, and two female IDU were infected with HIV B subtypes. Among heterosexual male IDU, five out of six (83.3%) men were infected with HIV CRF01_AE, and only one out of 12 (8.3%) men infected with HIV B had sexual contact history with FSW ($p < 0.01$) (Chen *et al.*, 2001b). Therefore, sexual transmission is a major risk factor of male IDU infected with HIV CRF01_AE in Taiwan.

ISSUES RELATED TO TREATMENT AND CARE

In Taiwan, the AIDS Control Law was launched in 1990 and has been modified five

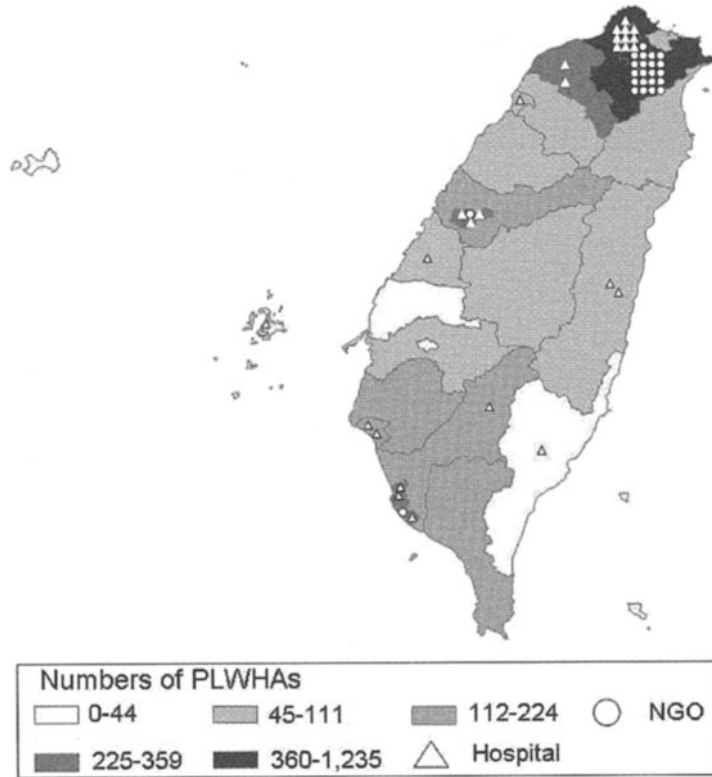


FIGURE 5. The distributions of AIDS designated hospitals and non-governmental organizations against the density of PLWHA in different prefectures and cities in Taiwan.

times since then. Under this law, the government has to provide free treatment to all Taiwanese PLWHA. Currently, there are 27 designated AIDS hospitals in Taiwan. As shown in Figure 5, the distribution of the hospitals is not even and some prefectures and cities do not have an AIDS hospital. The designated AIDS hospital system should be expanded to meet the medical needs of patients.

Highly Active Anti-Retroviral Therapy

Since April 1997, the Taiwanese government has provided protease inhibitors in conjunction with NRTIs (Nucleoside Reverse Transcriptase Inhibitors) and NNRTIs (Non-Nucleoside Reverse Transcriptase Inhibitors). The cost of the highly active anti-retroviral therapy (HAART) is about US\$ 1000 per

person per month. According to the Bureau of the National Health Insurance (BNHI), by the end of 2002, 2660 of 3425 (77.7%) PLWHA had begun receiving HAART. The implementation of the free HAART program in Taiwan has caused dramatic decreases of both morbidity and mortality of HIV/AIDS in Taiwan. A five-year prospective study on a cohort of 309 PLWHA (83% with AIDS) admitted to a teaching hospital in Taipei City showed that the mortality rate declined significantly from 110.5–148.4 per 100 patient-years in 1995 to 5.5–7.4 per 100 patient-years in 1999 (Hung *et al.*, 2000). The five leading HIV-associated opportunistic infections (OI) in the cohort were oroesophageal candidiasis, Pneumocystis carinii pneumonia, tuberculosis, mucocutaneous herpes simplex infection and cytomegalovirus diseases (Hung *et al.*, 2000).

The clinical spectrum of HIV/AIDS patients in Taiwan was very similar to that in the Western countries, but the incidence of OI differed, e.g. the incidence of tuberculosis in patients with advanced illness (24.6%) was relatively high, and the rate of an endemic fungal infection (*Penicillium marneffei* infection) was increasing (Hsieh *et al.*, 1996; Hsueh *et al.*, 2000).

HIV Drug Resistance

Although the BNHI provided free viral load and CD4 cell counts tests, the cost for genotyping of HIV drug resistance was not covered. Recently, we investigated the prevalence of HIV genotypic mutations in retrospective samples collected between 1997 and 2000. The results showed that among 136 treatment naïve PLWHA, none of the 31 MSM, 32 bisexual males, seven females, or four IDU had any primary mutation, while two of 62 (3.2%) MSM had M184V mutation for RT inhibitors (Elbeik *et al.*, 2002).

Non-Governmental Organizations and Social Movement

In response to the challenge of HIV/AIDS, since 1992, there have been 15 non-governmental organizations (NGOs) established in Taiwan to provide shelter, counseling, anonymous testing, social care, and education for PLWHA, vulnerable groups, and the general public. As shown in Figure 5, there is only one NGO in the middle region of the country and one in the southern part of Taiwan. It is worth mentioning that although there is no PLWHA NGO in Taiwan, a PWA Rights' Advocacy Association (PRAA) was established in 1997.

Issues on the Human Rights of PLWHA

In 1999, a survey was conducted to understand the human rights issues of PLWHA in Taiwan. Social workers from four

NGOs—the Living with Hope Organization, Taiwan Hemophilic PWA Association, PRAA, and Lourdes Home—were trained to be interviewers. In total, 50 PLWHA (45 men and five women) participated in the survey. The results showed that 16% had suffered from discrimination by medical staff and 30% had been refused or delayed when they sought medical care. In terms of education rights, our 1999 survey showed that two PLWHA were expelled and three were refused admission by school authorities. Because of their HIV status, three had lost their jobs, three had been offered early retirement, five had lost their prospects for promotion, and 22 had experienced harassment from their employers. Three patients stated that their children had been taken away from them when they revealed their status. At present, Taiwanese PLWHA are still restricted from taking tests to become government employees and professional technologists.

In 2002, a survey of 1292 medical personnel from 42 hospitals island-wide showed that 42.9% are not willing to care for PLWHA and 97.6% think there should be a law forcing PLWHA to disclose their seropositive status to medical personnel (Taiwan Root Medical Peace Corps, 2002).

To change the attitude of the general public toward PLWHA, family members of PLWHA and volunteers were invited to participate in a floating lantern ceremony at a riverside in Taipei City on World AIDS day in 1994. This memorial has become an annual event since then. In 1995, Taiwan invited the Names Project to bring 576 AIDS quilts for a special exhibition at the Chiang Kai-Shek memorial plaza on World AIDS day. The Taiwan AIDS Memorial Quilt Project was established under the Living with Hope Organization in 1995. In 2001, Taiwan invited the Photographer Network to show the "Positive lives" of PLWHA from different Asian countries. The images created, of pink and white lanterns floating on a river, and colorful quilts displayed in front of traditional Chinese

theaters, have shocked and moved many people in Taiwan.

CONCLUSION

In conclusion, the HIV/AIDS epidemic in Taiwan is evolving. There are several issues that need to be addressed immediately: sentinel surveillance of HIV infection among different high-risk groups should be implemented; prenatal counseling for the HIV antibody test and chemoprevention of mother-to-child transmission should be instituted immediately; and NGOs should receive more financial support from both the Taiwanese government and international agencies.

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