計畫編號：DOH 95 -DC- 1037

行政院衛生署疾病管制局九十五年度科技研究發展計畫

臺灣地區愛滋病毒感染高危險群的男同性戀者阿米巴原蟲感染前瞻性研究：強調致病性阿米巴原蟲的帶原率與介入性衛教對於阿米巴感染與愛滋病毒感染的影響

研 究 報 告

執行機構：台大醫學院附設醫院內科部

計畫主持人：洪健清

研究人員：

執行期間：95 年 1 月 1 日至 95 年 12 月 31 日

＊本研究報告僅供參考，不代表衛生署疾病管制局意見＊

目　　錄

研究報告中文摘要：

中文關鍵詞(至少三個)：致病性阿米巴原蟲、痢疾阿米巴原蟲、阿米巴原蟲感染、台灣

在民國九十三年一月到九十五年六月間，共有 359 位感染者送糞便檢查。我們發現 14 (3.9%)個檢體中帶有致病性阿米巴原蟲；相對於其他愛滋病毒感染風險族群，男同性戀感染者發生腸道致病性阿米巴原蟲感染的機會高達 6.453 倍之多 (95% 信賴區間, 0.8293, 50.22; P=0.07。針對 647 位初次血清檢查阿米巴抗體陰性的愛滋病毒感染者，我們利用感染者在門診中定期所抽取的血液檢體重新檢驗阿米巴抗體，我們發現 21 位(3.2%)由陰性轉為陽性。顯示最近曾經感染致病性阿米巴原蟲。這 21 位都是男同性戀者，佔所有男同性戀者的 5.1% (21/413)；相對 213 位異性戀感染者，並無一人發生抗體陽轉 (P=0.0004)。其次，259 位初次檢查並未發生致病性阿米巴原蟲感染的人追蹤糞便的檢查，我們發現 7 位(2.7%)發生新的感染。相對於其他愛滋病毒的感染風險群，男同性戀者發生新的阿米巴原蟲感染的風險是 3.882 (95% 信賴區間,, 0.4605, 32.731; P=0.35)。我們的追蹤研究顯示：愛滋病毒感染者患之痢疾阿米巴原蟲感染的盛行率與發生率仍然以男同性戀患者最高。

Abstract:

Key words: invasive amebiasis; *Entamoeba histolytica*; indirect hemagglutination; amebic infection; HIV-1 infection

Background Epidemiology of *Entamoeba histolytica* infection has rarely been described before in patients with immunosuppression from human immunodeficiency virus type 1 (HIV) infection, although *E. histolytica* infection is an increasingly important parasitic infection in HIV-infected patients in the East Asian region.

Methods The prevalence of *E. histolytica* infection among HIV-infected patients seeking medical care between January 2004 and July 2006 and free of gastrointestinal symptoms was investigated in stool samples of 359 patients using a specific amebic antigen test followed by a polymerase chain reaction and in blood samples from 192 HIV-infected patients using indirect hemagglutination (IHA) assay. The incidence of *E. histolytica* infection was investigated in serial stool and blood samples from 259 and 647 HIV-infected patients, respectively, who were enrolled between 1994 and 2005 and had not been diagnosed with *E. histolytica* infection before.

Results Between January 2004 and July 2006, 14 (3.9%) stool samples from 359 patients contained *E. histolytica*. The prevalence of *E. histolytica* infection among men

having sex with men (MSM) was 12/237 (5.1%), compared with 1 of 121 (1.0%) patients of other risk groups (odds ratio, 6.453; 95% confidence interval [95% CI], 0.8293, 50.22; P=0.07). During the same study period, 23 of 186 (12.4%) patients were seropositive for anti-amebic antibodies, all being MSM. Twenty-one (3.2%) of 647 patients who were seronegative for *E. histolytica* infection at baseline seroconverted after a median interval of 1507 days (range, 350-2546 days). The sero-incidence of *E. histolytica* infection among MSM was 5.1% (21/413) compared with 0% (0/203) among heterosexuals (P=0.0004). Seven (2.7%) of 259 who had more than two stool examinations were found to be infected with *E. histolytica*; the incidence of new *E. histolytica* infection among MSM was 3.8% (6/159) compared with 1.0% (1/100) among patients of other risk groups (odds ratio, 3.882; 95% CI, 0.4605, 32.731; P=0.35). Five of 8 (62.5%) seroconverted who were all MSM and acquired new *E. histolytica* infection, compared with 1 of 223 (0.4%) who did not acquire new infection (odds ratio, 370; 95% CI, 32.56, 4240).

Conclusions MSM who were HIV-infected in Taiwan was at higher risk of acquisition of *E. histolytica* than HIV-infected patients with other risks for HIV transmission.

【前言】

Invasive amebiasis (IA) is the second most common cause of mortality due to parasite infections worldwide, accounting for 40,000 to 100,000 deaths annually. High risk populations for developing IA include infants, pregnant women, and patients who are taking immunosuppressives [1, 2]. Interestingly, IA has not been considered to occur at a higher frequency in HIV-infected patients [3, 4]. In industrialized countries, the rare occurrence of IA in HIV-infected patients or persons at risk for HIV infection [4-9] is probably attributable to rare intestinal carriage of *E. histolytica*. This is in contrast with relatively frequent carriage of *E. dispar*, which is non-pathogenic among men who have sex with men (MSM) who attend sexually transmitted diseases clinics [10-13]. In a large study of more than 34,000 HIV-infected patients based on retrospective review of medical records in the US [9], 111 (0.3%) patients were diagnosed as having *E. histoytica* or *E. dispar* infection, and only 2 had extraintestinal amebiasis. MSM and patients from endemic areas of *E. histolytica* infection were significantly associated with amebiasis. However, the interpretation of the results of this study is limited by retrospective study design and failure to differentiate between *E. histolytica* and *E. dispar* [14].

In developing countries, the studies of enteric infections due to amebas yielded inconsistent results in HIV-infected persons compared with HIV-uninfected persons [15-22]. The interpretation of these studies, however, is difficult because in almost all of the studies the diagnosis of amebiasis was based solely on microscopic examination of stool samples which is an insensitive test that fails to distinguish *E. histolytica* from *E. dispar* [14]. In a cross-sectional study using stool antigen detection and polymerase chain reaction (PCR) from Mexico where amebiasis is endemic,

investigators found that HIV-infected patients appeared to have a higher rate, though not statistically significant, of *E. histolytica* infection than their sexual partners or close contacts [23]. However, those patients colonized with *E. histolytica* did not develop invasive diseases over the 12-month follow-up period.

Over the past few years, we and many investigators have found that IA is increasingly diagnosed among HIV-infected MSM in Japan, Taiwan, and Korea [24-31]. Of the estimated more than 600 reported cases of amebiasis annually in Japan, 80% of them occur in MSM [32]. A substantial proportion of them with IA are also co-infected with HIV and syphilis [24, 30]. In Taiwan, approximately 5-6% of HIV-infected patients develop IA, in many of whom IA is the presenting disease of HIV infection [31]. Serologic surveys in the US, Italy, Japan and Taiwan also demonstrate that MSM, HIV-infected or not, are at increased risk of exposure to *E. histolytica* with positive anti-amebic serologies [13, 26, 31, 33-35]. Oral-anal sexual contact has been found to be significantly associated with acquisition of such infection [36].

Although IA has been considered an increasingly important parasitic infection in HIV-infected patients in three East Asian countries, we do not know the seroconversion rate against *E. histolyitca* and its risk factors. In this study, we conducted a survey to assess the prevalence and incidence of *E. histolytica* infection among persons with HIV infection at a referral medical center for HIV care in northern Taiwan.

【材料與方法】

Sero-prevalence and sero-incidence of *E. histolytica* infection

The IHA assay was routinely performed in patients who first sought medical attention and in patients with diarrhea and hepatic tumors at NTUH. Serum samples collected from HIV-infected patients who were IHA seronegative at baseline and who were still in clinic follow-up in June 2006 were retested to determine the sero-incidence of *E. histolytica* infection. The interval between the two blood samples were at least one year. In those found to be seropositive at the last clinic follow-up or the end date of the study (June 2006), serially stored serum samples were tested retrospectively to determine the seroconversion time.

Cross-sectional and longitudinal survey of *E. histolytica* infection

Stool samples from HIV-infected persons were tested for the presence of stool *Entamoeba* antigen using TechLab commercial test kits (ENTAMOEBA TEST, TechLab, Branchburg, NJ) between 1 January, 2004 and 30 June, 2006. Positive samples were further tested by PCR to differentiate between *E. histolytica* and *E. dispar*. The PCR methods were as described previously [31].

A repeat stool antigen test and PCR test was performed in patients with a negative test result at baseline in order to assess the incidence of *E. histolytica* infection. The study protocol was approved by the Institutional Review Board of NTUH.

Statistical analysis

All statistical analyses were performed using SAS statistical software (Version 8.1, SAS Institute Inc., Cary, NC, U.S.A.). Categorical variables were compared using χ^2 or

Fisher's exact test whereas noncategorical variables were compared using Wilcoxon's rank-sum test. A multivariate analysis was performed to identify risk factors associated with IA or presence of high IHA titers. Odds ratios and 95% confidence intervals (95% CI) were also calculated. All tests were two-tailed. A p value <0.05 was considered significant.

The appropriate sample size of the intestinal colonization study was based on the estimate of 15% intestinal carriage rate of *E. histolytica*/*E. dispar*, taking into account the precision of 0.04 (95% CI, 11%, 19%).

【結果】

Sero-prevalence and sero-incidence of *E. histolytica* infection

During the 12-year study period, 69 (6.8%) of 1021 HIV-infected patients were seropositive for *E. histolytica* infection: 6.9% between 1994 and 2003 was and 6.8% between 2004 and 2006 (p=0.99) (Table 1). In patients enrolled in both study periods, sero-prevalence was significantly higher in MSM than in other risk groups for HIV transmission (Table 1).

Six hundred and forty-seven patients who were *E. histolytica* seronegative at baseline and had a second blood sample available were enrolled in the sero-incidence study using the same IHA assays. The median interval between the two blood samples was 1012 days (range, 350-4316 days). Twenty-one (3.2%) of the 647 HIV-infected patients seroconverted; the median seroconverting interval was 1507 days (range, 350-2546 days). The sero-incidence of *E. histolytica* infection among MSM was 5.1% (21/413) compared with 0% (0/203) among heterosexuals (P=0.0004).

Cross-sectional and longitudinal survey of intestinal colonization with *E. histolytica*

Three hundred and fifty-nine patients with HIV infection who had no gastrointestinal symptoms submitted stool samples for *E. histolytica* antigen tests between January 2004 and July 2006; 237 were MSM, 103 heterosexuals, and 19 intravenous drug user or patients with another transmission risk factor. In 14 (3.9%) of the 359 patients stool samples contained *E. histolytica*. Twelve (5.1%) of 237 MSM were infected with *E. histolytica*, compared with 1 of 122 (0.8%) heterosexuals (odds

ratio, 6.453; 95% CI, 0.8293, 50.22; P=0.07).

Two hundred and fifty-nine patients with HIV infection submitted more than two stool samples for *E. histolytica* antigen testings between January 2004 and June 2006; 159 were MSM, 92 heterosexuals, and 8 patients with another HIV transmission risk factor. Seven (2.7%) of the 259 patients were found to be infected with *E. histolytica*; the incidence of a new infection among MSM was 3.8% (6/159), compared with 1.0% (1/100) among patients of other risk groups (odds ratio, 3.882; 95% CI, 0.4605, 32.731; P=0.35). The median interval between the negative stool antigen tests and positive antigen tests of the 7 patients was 427 days (range, 85-787).

We also assessed whether seroconversion was associated with new acquisition of *E. histolytica* infection among all of the patients who submitted two or more stool samples. Five of 8 (62.5%) who were all MSM and seroconverted acquired new *E. histolytica* infection, compared with 1 of 223 (0.4%) who did not seroconvert (odds ratio, 370; 95% CI, 32.56, 4240).

【討論】

Our survey of *E. histolytica* infection and IA among HIV-infected patients who sought HIV care at a university hospital confirmed our previous cross-sectional study that MSM were associated with a significantly higher risk for *E. histolytica* infection and development of IA [31].

Exposure to *E. histolytica*, but not *E. dispar*, may induce anti-amebic antibody response. Therefore, development of anti-antibodies may be representative of recent or remote exposure to *E. histolyica* infection [14, 40], although not every person infected with *E. histolytica* develops antibody response. Such a test can be used as a tool to understand the epidemiology of *E. histolytica* among high-risk populations. In this study, we chose a high titer of 128 as the cut-off value which decreases the possibility of cross-reactions. For the study of intestinal carriage of *E. histolytica*, we used a sensitive tool followed by PCR, which allowed us to differentiate between *E. histolytica* and *E. dispar*.

In the first survey of HIV-infected patients who sought HIV care between 1994 and 2003 (Table 1), we found that seroprevalence of *E. histolytica* infection was 6.9% and 52 (5.4%) patients were diagnosed with IA [31]. Our second survey demonstrated a similar seroprevalence (6.3%) in patients enrolled in 2004-2006 (Table 1). Both surveys showed that MSM had the highest seroprevalence of *E. histolytica* infection compared with other risk groups, with an adjusted odds ratio of 4.462 (95% CI, 1.607-12.395) [31]. Even compared with HIV-uninfected persons with gastrointestinal symptoms who had their sera tested for *E. histolytica* infection, the risk for *E. histolytica* infection among HIV-infected patients remained significantly higher, with an odds ratio of 3.206 (95% CI, 1.433, 7.176) (p=0.005) after adjustments [34].

The findings of higher seroprevalence of *E. histolytica* infection among MSM in both study periods were consistent with surveys in MSM in the US [13] and in MSM who attended gay sauna bars in Taiwan in 2004 [35] (Table 3), which found that 5.7% of MSM were seropositive for *E. histolytica*, although it was lower than the seroprevalence of MSM detected by Italian and Japanese investigators, who found a significantly higher prevalence in MSM (13.4-20.4%) than in heterosexuals (1.0%) and prostitutes (0.8%) [24-26, 33]. Of the stool samples from 332 asymptomatic HIV-infected patients, the prevalence of *E. histolytica*/*E. dispar* by stool antigen tests was 12.1% (40/332), compared with 1.4% (2/178) healthy controls; 25% of the 40 isolates from HIV-infected persons were identified as *E. histolytica* by PCR [31]. Although the majority of persons infected with *E. histolytica* are asymptomatic [1, 2], more than 80% of the 600 or greater annually reported cases of amebiasis in Japan occurring in MSM [32] may reflect the dimension of the *E. histolytica* infection in developed countries where improvement of public hygiene and sanitation has reduced the risk of acquisition of *E. histolytica* through contaminated water or food.

Sharing the identical transmission route with *E. histolytica*, the transmission of *E. dispar* among MSM in developed countries is correlated with oral-anal sexual contact, and 20-40% of MSM who attended sexually transmitted diseases clinic were found to be infected with *E. dispar* [10-12]. Therefore, infection with either *E. dispar* or *E. histolytica* is indicative of unsafe oral-anal sexual contact among MSM. In both incidence studies, we further demonstrated that HIV-infected MSM were more likely than other risk groups to acquire *E. histolytica* during follow-up, though not statistically significantly different due to smaller sample size. Nearly 4% of HIV-infected MSM acquired *E. histolytica* and 5% of MSM seroconverted, compared with 1.0% and 0% among patients of other risk groups, respectively. These findings highlight the

importance of counseling regarding transmission of HIV and other sexually transmitted agents that precautions are necessary to prevent *E. histolytica* infection through oral-anal sexual contact.

There are several limitations of our study and generalization of our findings to areas with similar socio-economic development should be cautious. First, the risk for exposure to *E. histolytica* is low in Taiwan as reflected by the low seroprevalence (0.12%) of *E. histolytica* infection among 2500 healthy controls in a recent survey in northern and southern Taiwan [34]. IA is a reportable infectious disease which is mainly diagnosed in persons who reside in institutions for mentally retarded and HIV-infected patients in Taiwan. Between 2005 and 2006, 40% of the cases reported to Center for Disease Control, Taiwan were HIV-infected MSM [Ji DD, personal communication]. The higher proportion of HIV-infected MSM may be related to heightened awareness of the interactions between MSM and amebiasis after revision of structured questionnaire interview in 2005 when MSM was listed as a risk factor for development of IA. Second, our study is limited by selection bias. Most patients at late stage of HIV infection who develop HIV-related complications are referral to this hospital, as demonstrated by the low CD4 counts at baseline of the 1373 patients seen over the past 12 years (Table 1). However, those patients with IA had significantly higher CD4 counts than the patients without, which suggests that *E. histolyica* infection may not be associated with immunosuppression in HIV-infected patients. It is the risky behavior that increases risk of *E. histolyica* infection and subsequent development of invasive diseases. Third, our study was limited by the small sample size in assessment of the incidence of *E. histolytica* infection by stool antigen assays during follow-up. Although the incidence of *E. histolytica* infection is higher in MSM than in heterosexuals and others, the difference does not reach

statistical significance. The shedding of *E. histolytica* may be intermittent which may reduce the sensitivity of antigen assays if only one stool samples are tested. The stool samples may not be collected at the pre-defined time periods, which may prevent us from estimating the incidence rate of infection. However, combination with IHA assays for *E. histolytica* infection in our study may compensate for the deficiency by increasing the detection sensitivity.

.

【結論與建議】

In conclusion, MSM who are HIV-infected in Taiwan are at higher risk of acquisition of *E. histolytica* than other HIV-infected patients with other risks for HIV transmission.

95 年度計畫重要研究成果及具體建議

（本資料須另附乙份於成果報告中）

計畫名稱：臺灣地區愛滋病毒感染高危險群的男同性戀者阿米巴原蟲感染前瞻性研究：強調致病性阿米巴原蟲的帶原率與介入性衛教對於阿米巴感染與愛滋病毒感染的影響

主 持 人：洪 健 清　　計畫編號：DOH95-DC-1037

1.計畫之新發現或新發明

台灣地區男同性戀的愛滋病毒感染者是發生致病性阿米巴原蟲的高風險群

2.計畫對民眾具教育宣導之成果

3.計畫對醫藥衛生政策之具體建議

建議未來針對醫事人員的持續教育和男同性戀者的衛生教育中，強調新的痢疾阿米巴的感染途徑，並且針對社區中散發的侵犯性阿米巴感染的對象流行病學調查中加入了性行為和接觸對象的追蹤。

【參考文獻】

1. Haque R, Huston CD, Hughes M, Houpt E, Petri WA Jr. Amebiasis. N Engl J Med 2003;348:1565-73.
2. Stanley SL Jr. Amoebiasis. Lancet 2003;361:1025-34.
3. Lucas SB. Missing infections in AIDS. Trans R Soc Trop Med Hyg 1990;84 (Suppl 1):34-8.
4. Reed SL, Wessel DW, Davis CE: *Entamoeba histolytica* infection and AIDS. Am J Med 1991;90:269-71.
5. Smith PD, Lane HC, Gill VJ, Manischewitz JF, Quinnan GV, Fauci AS, Masur H: Intestinal infections in patients with the acquired immunodeficiency syndrome (AIDS). Etiology and response to therapy. Ann Intern Med 1988;108:328-333.
6. Blanshard C, Collins C, Francis N, Gazzard BG. Invasive amoebic colitis in AIDS patients. AIDS 1992;6:1043-1044.
7. Fatkenheuer G, Arnold G, Steffen HM, Franzen C, Schrappe M, Diehl V, Salzberger B. Invasive amoebiasis in two patients with AIDS and cytomegalovirus colitis. J Clin Microbiol 1997;35:2168-2169.
8. Weber R, Ledergerber B, Zbinden R, Altwegg M, Pfyffer GE, Spycher MA, Briner J, Kaiser L, Opravil M, Meyenberger C, Flepp M. Enteric infections and diarrhea in human immunodeficiency virus-infected persons: prospective community-based cohort study. Swiss HIV Cohort Study. Arch Intern Med. 1999;159:1473-80.
9. Lowther SA, Dworkin MS, Hanson DL, and the Adult and Adolescent Spectrum of Human Immunodeficiency Virus Disease Project: *Entamoeba histolytica*/*Entamoeba dispar* in human immunodeficiency virus-infected patients in the United States. Clin Infect Dis 2000;30:955-959.
10. Phillips SC, Mildvan D, William DC, Gelb AM, White AC: Sexual transmission of

enteric protozoa and helminths in a venereal-disease-clinic population. N Engl J Med 1981;305:603-606.

11. Quinn TC, Stamm WE, Goodell SE, Mkrtichian E, Benedetti J, Corey L, Schuffler MD, Holmes KK: The polymicrobial origin of intestinal infections in homosexual men. N Engl J Med 1983;309: 576-582.
12. Allason-Jones E, Mindel A, Sargenunt P, Williams P: *Entamoeba histolytica* as a commensal intestinal parasite in homosexual men. N Engl J Med 1986;315: 353-356.
13. Sorvillo FJ, Strassburg MA, Seidel J, Visvesvara GS, Mori K, Todd A, Portigal L, Finn M, Agee BA. Amebic infections in asymptomatic homosexual men, lack of evidence of invasive disease. Am J Public Health 1986;76:1137-9.
14. Tanyuksel M, Petri WA Jr. Laboratory diagnosis of amebiasis. Clin Microbiol Rev 2003;16:713-29.
15. Gomez Morales MA, Atzori C, Ludovisi A, Rossi P, Scaglia M, Pozio E. Opportunistic and non-opportunistic parasites in HIV-positive and negative patients with diarrhoea in Tanzania. Trop Med Parasitol 1995;46:109-14.
16. Germani Y, Minssart P, Vohito M, Yassibanda S, Glaziou P, Hocquet D, Berthelemy P, Morvan J. Etiologies of acute, persistent, and dysenteric diarrheas in adults in Bangui, Central African Republic, in relation to human immunodeficiency virus serostatus. Am J Trop Med Hyg 1998;59:1008-14.
17. Fontanet AL, Sahlu T, Rinke de Wit T, Messele T, Masho W, Woldemichael T, Yeneneh H, Coutinho RA. Epidemiology of infections with intestinal parasites and human immunodeficiency virus (HIV) among sugar-estate residents in Ethiopia. Ann Trop Med Parasitol 2000;94:269-78.
18. Waywa D, Kongkriengdaj S, Chaidatch S, Tiengrim S, Kowadisaiburana B,

Chaikachonpat S, Suwanagool S, Chaiprasert A, Curry A, Bailey W, Suputtamongkol Y, Beeching NJ. Protozoan enteric infection in AIDS related diarrhea in Thailand. Southeast Asian J Trop Med Public Health 2001;32 (Suppl 2):151-5.

19. Mohandas K, Sehgal R, Sud A, Malla N. Prevalence of intestinal parasitic pathogens in HIV-seropositive individuals in Northern India. Jpn J Infect Dis 2002;55:83-4.
20. Senya C, Mehta A, Harwell JI, Pugatch D, Flanigan T, Mayer KH. Spectrum of opportunistic infections in hospitalized HIV-infected patients in Phnom Penh, Cambodia. Int J STD AIDS. 2003;14:411-6.
21. Hailemariam G, Kassu A, Abebe G, Abate E, Damte D, Mekonnen E, Ota F. Intestinal parasitic infections in HIV/AIDS and HIV seronegative individuals in a teaching hospital, Ethiopia. Jpn J Infect Dis 2004;57:41-3.
22. Sadraei J, Rizvi MA, Baveja UK. Diarrhea, CD4+ cell counts and opportunistic protozoa in Indian HIV-infected patients. Parasitol Res 2005;97:270-3.
23. Moran P, Ramos F, Ramiro M, Curiel O, Gonzalez E, Valadez A, Gomez A, Garcia G, Melendro EI, Ximenez C: Infection by human immunodeficiency virus-1 is not a risk factor for amebiasis. Am J Trop Med Hyg 2005;73:296-300.
24. Takeuchi T, Kobayashi S, Asami K, Yamaguchi N. Correlation of positive syphilis serology with invasive amebiasis in Japan. Am J Trop Med Hyg 1987;36:321-4.
25. Takeuchi T, Miyahira Y, Kobyash S, Nozaki T, Motta S, Matsuda L: High seropositivity for *Entamoeba histolytica* infection in Japanese homosexual men: further evidence for occurrence of pathogenic strains. Trans R Soc Trop Med Hyg 1990;84: 250-251.
26. Takeuchi T, Okuzawa E, Nozaki T, Kobayashi S, Mizokami M, Minoshima N,

Yamamoto M, Isomura S: High seropositivity of Japanese homosexual men for amebic infection. J Infect Dis 1989;159: 808.

27. Ohnishi K, Murata M. Present characteristics of symptomatic amebiasis due to *Entamoeba histolytica* in the east-southeast area of Tokyo. Epidemiol Infect 1997;119:363-7.

28. Hung CC, Chen PJ, Hsieh SM, et al. Invasive amebiasis: an emerging parasitic disease in patients with HIV infection in an endemic area of amebic infection. AIDS 1999;13:2421-2428.

29. Oh MD, Lee K, Kim E, Lee S, Kim N, Choi H, Choi MH, Chai JY, Choe K. Amoebic liver abscess in HIV-infected patients. AIDS 2000;14:1872-3.

30. Ohnishi K, Kato Y, Imamura A, Fukayama M, Tsunoda T, Sakaue Y, Sakamoto M, Sagara H. Present characteristics of symptomatic *Entamoeba histolytica* infection in the big cities of Japan. Epidemiol Infect 2004;132:57-60.

31. Hung CC, Deng HI, Hsiao WH, Hsieh SM, Hsiao CF, Chen MY, Chang SC, Su KE. Invasive amoebiasis is an emerging parasitic infection in patients with HIV infection. Arch Intern Med 2005;165:409-415.

32. Nozaki T, Kobayashi S, Takeuchi T, Haghighi A. Diversity of clinical isolates of *Entamoeba histolytica* in Japan. Arch Med Res 2006;37:277-9.

33. Aceti A, Pennica A, Ippolito G, Moretto D, Rezza G, Titti F, Perucci CA: Antiamebic antibodies in homosexual men. N Engl J Med 1987;316: 692.

34. Tsai JJ, Sun HY, Ke LY, Tsai KS, Chang SY, Hsieh SM, Hsiao CF, Yen JJ, Hung CC, Chang SC: Higher seroprevalence of *Entamoeba histolytica* infection is associated with human immunodeficiency virus Type 1 infection in Taiwan Am J Trop Med Hyg 2006;74:1016-9.

35. Ko NY, Lee HC, Chang JL, Lee NY, Chang CM, Lee MP, Lin YH, Lai KY, Ko WC:

Prevalence of human immunodeficiency virus and sexually transmitted infections and risky sexual behaviors among men visiting gay bathhouses in Taiwan. Sex Transmitted Dis 2006;33:467-73.

36. Keystone JS, Keystone DL, Proctor EM: Intestinal parasitic infections in homosexual men: prevalence, symptoms and factors in transmission. CMAJ 1980;123: 512-514.
37. Wei SJ, Hung CC, Chen MY, Wong CI, Chuang CY, Wong JM: Endoscopy in AIDS patients with diarrhea of negative non-invasive studies. Gastrointest Endoscopy 2000;51: 427-432.
38. Liu CJ, Hung CC, Chen MY, et al. Amebic liver abscess and human immunodeficiency virus infection: a report of three cases. J Clin Gastroenterol 2001;33:64-68.
39. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep 1992;41:1-19.
40. Gathiram V, Jackson TFHG: A longitudinal study of asymptomatic carriers of pathogenic zymodemes of *Entamoeba histolytica*. S Afr Med J 1987,72:669-72.

Table 1. Baseline characteristics of HIV-infected patients with invasive amebiasis diagnosed between 1994 and 2006

	A: 1994-2003	B: 2004-2006	1994-2006	Statistics A vs. B
Patients enrolled	968	405	1373	
Age, median (range), y	33 (15-83)	35 (17-93)	34 (15-93)	0.84
Sex, M/F	896/72 (12.4)	367/38 (9.7)	1263/110 (11.5)	0.23
Risk factor for HIV transmission, (%)				
Homosexual/bisexual	587 (60.6)	266 (65.7)	853 (62.1)	<0.0001
Heterosexual	317 (32.7)	63 (15.6)	380 (27.7)	
IDU	20 (2.1)	55 (13.6)	75 (5.5)	
Others	44 (4.5)	20 (4.9)	64 (4.7)	
CD4 count, median (range) $x10^6$/L	71 (0-1202)	200 (0-988)	96 (0-1202)	<0.0001
CD4<200 $x10^6$/L (%)	615/906 (67.8)	192/387 (49.6)	807/1293 (62.4)	<0.0001
# Invasive amebiasis diagnosed, (%)	52 (5.4)	12 (3.0)	64 (4.7)	0.05
Homosexual/bisexual	*42/587 (7.2)	**12/267 (4.1)	***54/854 (6.2)	0.17
Heterosexual	10/317 (3.2)	0/63 (0)	10/380 (2.6)	0.23
Others	0/64 (0)	0/75 (0)	0/139 (0)	1.00
CD4 count at diagnosis of invasive amebiasis, median (range) $x10^6$/L	208.5 (6-805)	208 (26-428)	215 (6-805)	0.87
CD4<200 $x10^6$/L (%)	20/44 (45.5)	6/12 (50.0)	26/56 (46.4)	1.00
## Patients with IHA≧128, n/N (%)	57/830 (6.9)	13/191 (6.8)	69/1021 (6.8)	0.99

Homosexual/bisexual	*49/531 (9.2)	**12/130 (9.2)	***61/661 (9.2)	0.99
Heterosexual	6/260 (2.3)	1/31 (3.2)	7/291 (2.4)	0.99
IDU	1/16 (6.3)	0/14 (0)	1/30 (3.3)	0.99
Others	1/23 (4.3)	0/16 (0)	1/39 (2.6)	0.99
IHA titer				
≧128	57 (6.9)	13 (6.8)	69 (6.8)	0.88
32-64	14 (1.7)	2 (0.5)	16 (1.6)	
<32	759 (91.4)	171 (89.5)	926 (90.7)	

IDU: intravenous drug user; IHA: indirect hemagglutination

Homosexual/bisexual versus other risks in the same study period: *p=0.002; **p=0.01; ***p=0.002

##Homosexual/bisexual versus other risks in the same study period : *p=0.0002; **p=0.09; ***p=0.0000

Figure 1. Study population of HIV-infected patients at the NTUH, 1994-2006