

Prevalence of Human Immunodeficiency Virus and its Association With Hepatitis B, C, and D Virus Infections Among Incarcerated Male Substance Abusers in Taiwan

Fang-Yeh Chu,^{1,2,3} Shu-Chuan Chiang,^{4,5,6} Fu-Hsiung Su,² Yuan-Ying Chang,⁷ and Shu-Hsing Cheng^{8,9*}

¹Department of Clinical Pathology, Far Eastern Memorial Hospital, Pan-Chiao, Taipei, Taiwan

²Department of Family Medicine, Far Eastern Memorial Hospital, Pan-Chiao, Taipei, Taiwan

³Department of Medical Laboratory Science and Biotechnology, College of Biomedical Science and Technology, Yuanpei University, Hsinchu, Taiwan

⁴Institute of Public Health & Division of Preventive Medicine, National Yang-Ming University, Taipei, Taiwan

⁵Ching Yun University, Jung-Li, Taiwan

⁶Sunrise Clinic, Taoyuan, Taiwan

⁷Tzu-Li Clinic, Taoyuan, Taiwan

⁸Department of Infectious Diseases, Taoyuan General Hospital, Department of Health, Taoyuan, Taiwan

⁹School of Public Health, College of Public Health and Nutrition, Taipei Medical University, Taipei, Taiwan

Taiwan has been facing a rising epidemic of human immunodeficiency virus (HIV) infection since 2004. Injection drug users comprised 38.5% of accumulated HIV cases by 2007. This cross-sectional study investigated the seroprevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and HIV infection in 753 male substance users who were detained in a detoxification center in Taoyuan, Taiwan. The subjects were enrolled into the study consecutively between February and October, 2005. The seroprevalence rates of HIV antibodies, HCV antibodies, and HBV surface antigens among all subjects, and HDV antibodies among HBV carriers were 6.9% (95% confidence interval [CI]: 5.19–8.95), 30.5% (95% CI: 27.23–33.93), 16.9% (95% CI: 14.24–19.71) and 13.7% (95% CI: 8.19–21.04), respectively. Subjects in the heroin injection group had significantly higher rates of HIV infection, HCV infection and HDV superinfection (25.5%, 89.6%, and 38.7%) than those in the heroin non-injection group (0.9%, 24.5%, and 6.25%), the methamphetamine group (0.3%, 8.1%, and 6.7%), and the club drug group (1%, 3%, and 0%; $P < 0.001$). The odds of HCV, HIV, or HDV infection were 74.7, 63.8, and 11.1 higher, respectively, for heroin injection drug users than for non-injection drug users ($P < 0.0001$). Compared to HIV-negative individuals, the odds of being a heroin injector and the odds of HCV co-infections were 64-fold and 149-fold higher, respectively, in HIV-positive individuals. The impact of HBV, HCV, and HDV infection on the

HIV epidemic in Taiwan should be monitored closely. **J. Med. Virol.** 81:973–978, 2009.

© 2009 Wiley-Liss, Inc.

KEY WORDS: HIV; hepatitis; substance abuse; heroin; injections; Taiwan

INTRODUCTION

There are approximately 200 million substance abusers worldwide, and among them, 13.2 million are injection drug users. Over 10 million injection drug users (78%) live in developing countries [UNAIDS, 2003, 2004, 2005; Aceijas et al., 2004; Jarlais Des and Semaan, 2008]. It has been well documented that injection drug use contributes to the epidemic of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) [UNAIDS, 2004, 2003]. Studies in 2004 found that the prevalence of HIV infection among injection drug users was over 20% in 25 of the 78 countries surveyed [Aceijas et al., 2004]. Furthermore, the prevalence of HIV infection in injection drug

Grant sponsor: Taoyuan General Hospital, Department of Health (partial support); Grant number: DOH94-HO-2033; Grant sponsor (partial): Taoyuan Mental Hospital.

*Correspondence to: Shu-Hsing Cheng, MD, Department of Infectious Diseases, Taoyuan General Hospital, Department of Health, No. 1492, Chung-Shan Rd., Taoyuan 330, Taiwan. E-mail: shuhsingcheng@gmail.com

Accepted 4 February 2009

DOI 10.1002/jmv.21481

Published online in Wiley InterScience
(www.interscience.wiley.com)

users has reached epidemic proportions in sub-Saharan Africa, Eastern Europe, and Central Asia [UNAIDS, 2005].

HIV infection was first detected in Taiwan in 1984 in homosexual men. Since then, the number of people living with HIV/AIDS in Taiwan has a steady rate of increase, approximately 10–20% annually, until the year 2003 [Centers for Disease Control Taiwan, 2003]. The most common identifiable risk groups for infection with HIV in 2003 were heterosexual (41.3%), homosexual (39.5%), and bisexual (12.4%). At that time, only 2.1% of HIV-positive individuals were injection drug users [Centers for Disease Control Taiwan, 2003]. Thereafter, the proportion of newly diagnosed HIV-positive cases attributed to injection drug use increased markedly. There was a 77% increase in 2004, and a 110% increase in 2005 [Centers for Disease Control Taiwan, 2005]. At the end of 2007, there were approximately 15,000 HIV-positive patients in Taiwan, and 38.5% of them were injection drug users [Centers for Disease Control Taiwan, 2007].

Illicit drug users, including injection drug users, tend to have multiple risk factors for HIV infection, such as use of contaminated injection equipment, unprotected sex, tattooing, and trading sex in exchange for drugs [Kral et al., 2001; Nelson et al., 2002; Rosengard et al., 2004]. These risk factors are also common modes of transmission of hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis D virus (HDV). Previous studies have shown that patients with chronic viral hepatitis and HIV co-infection exhibited an accelerated progression to liver cirrhosis and hepatocellular carcinoma [Benhamou et al., 1999; Colin et al., 1999; Bica et al., 2001], and had a higher rate of liver-related mortality compared with patients with HIV monoinfection [Bonacini et al., 2004]. Thus, it is important to understand the prevalence of viral hepatitis among injection drug users and patients infected with HIV.

Injection drug abuse has been the most important contributor to the increase in HIV infection in Taiwan since 2004, and may have a significant impact on the prevalence of HBV, HCV, and HDV infections. Knowledge of the current prevalence of infections with HIV and other bloodborne pathogens among illicit drug users is of the utmost importance for determining the allocation of medical resources. This study investigated the prevalence of HIV, HCV, HBV, and HDV infections among illicit drug users in 2005, the year with the highest reported numbers of HIV infection in Taiwan.

METHODS

Patient Population

A total of 762 male illicit drug users in a detoxification center in Taoyuan, Taiwan were enrolled consecutively between February and October, 2005. Under Taiwanese law, drug use is a crime, and illicit drug users who are convicted of a first or second drug offence are incarcerated in a prison-affiliated detoxification center for 1 to 2 months. All detainees are tested for the

presence of HIV-I/II antibodies upon admission to the detention facility [Ministry of Justice Taiwan, 2005]. All of the participants in this study gave written informed consent to undergo additional tests for hepatitis B, C, and D (approved by the Committee on Human Research, Taoyuan Mental Hospital, Taoyuan, Taiwan). Data on demographic characteristics, including education level, family and marital status, and substance abuse history, including types and routes of substance use, were obtained from prison records. Data on personal information, including sexual activities and needle-sharing behaviors, were obtained from 121 subjects during face-to-face interviews conducted by trained staff using a questionnaire. All 121 subjects gave written informed consent to be interviewed. The subjects were classified according to the major substances used before incarceration into the following four groups: club drug group (3,4-methylenedioxymethamphetamine [MDMA], marijuana, or sedatives), methamphetamine group, heroin non-injection group, and heroin injection group.

Laboratory Methods

A total of 762 subjects had blood drawn for testing for HIV, HCV, HBV, and HDV infection. Nine subjects were excluded because of insufficient blood samples. Therefore, the final study population comprised 753 individuals. Immunoassays available commercially were used to test for viral hepatitis markers, including hepatitis B surface antigen (HBsAg), and antibodies to HDV, HCV, and HIV. Briefly, blood samples were collected by a medical technologist and then sent to the laboratory at the Taoyuan General Hospital, Taoyuan for examination within 2 hr. A microparticle enzyme immunoassay (MEIA, AxSYM HIV-1/2 gO, Abbott Diagnostic Division, Abbott Park, IL) was used to detect the HIV-I/II antibody. Samples with positive results were run in duplicate, and the results were confirmed by Western blot HIV-1 or HIV-2 assays (New LAV Blot-I and II, Bio-Rad Fugirebio, Inc., Tokyo, Japan). HCV antibody and HBsAg testing were performed by the MEIA method (AxSYM HCV version 3.0 and AxSYM HBsAg assay, Abbott Diagnostic Division). HDV antibody was detected by the enzyme-linked immunosorbent assay (ELISA, ETI-AB-DELTA-2, DiaSorin, Saluggia, Italy).

Statistical Analyses

Demographic data are presented as the mean \pm standard deviation for continuous variables and as a percentile for discrete variables. Prevalence rates of HIV, HCV, HBsAg, and HDV infections in each group were calculated, and the 95% Clopper-Pearson confidence bounds were estimated [Borkowf, 2006]. In univariate analysis, odds ratio comparing injection drug users and non-injection drug users, and HIV and non-HIV were calculated using the Fisher's exact test for 2×2 comparisons. The Chi square test was used for 2×3 or more comparisons when appropriate. A logistic regression analysis was also applied for the association

between variables and the various viral infections. A *P* value of less than 0.01 was considered statistically significant.

RESULTS

A total of 753 subjects were enrolled, including 192 heroin injectors, 106 heroin non-injectors, 356 methamphetamine users, and 99 club drug users. All of the heroin users (100%, 298/298), including injectors and non-injectors, also used methamphetamines. The mean age of the subjects was 30.4 ± 7.5 years (range, 16–57 years). The mean age of onset of illicit drug use was 23 ± 6 years for club drug, 26 ± 7 years for methamphetamine, 29 ± 6 years for heroin non-injection, and 31 ± 7 years for heroin injection. Demographic characteristics and the risk factors for bloodborne or sexual transmitted infections are summarized in Table I. Table I showed that the injection drug users had a significantly higher rate of sharing injection equipment ($P < 0.001$), compared with others.

The seroprevalence rates of anti-HIV, anti-HCV, and HBsAg among all subjects, and anti-HDV among HBsAg carriers in these male substance abusers were 6.9% (95% confidence interval [CI]: 5.19–8.95), 30.5% (95% CI: 27.2–33.93), 16.9% (95% CI: 14.24–19.71) and 13.7% (95% CI: 8.19–21.04), respectively. The rates of HIV and HCV infection and HDV superinfection were significantly higher in heroin injection group (25.5%, 89.6%, and 38.7%) than in heroin non-injection group (0.9%, 24.5%, and 6.25%), methamphetamine group (0.3%, 8.1%, and 6.7%), and club drug group (1%, 3%, and 0%; $P < 0.001$). The HBsAg-positive rate did not differ significantly between the four study groups (range, 16–17.2%; Table II). The odds of having HCV,

HIV, or HDV infection were 74.7 (95% CI: 43.7–127.8, $P < 0.0001$), 63.8 (95% CI: 19.6–207.8, $P < 0.0001$), and 11.1 (95% CI: 3.5–35.3, $P < 0.0001$) higher, respectively, for heroin injection drug users than for non-injection drug users in the logistic regression analysis.

Among the 52 HIV-positive cases, 49 (94.2%) were heroin injection users. Co-infections among the HIV-positive cases included HCV ($n = 51$, 98.1%), HBsAg ($n = 6$, 11.5%), and HDV superinfection ($n = 1$, 16.7%). The odds of being a heroin injector and the odds of having HCV co-infections were 64-fold (95% CI: 19.6–207.8, $P < 0.0001$) and 149-fold (95% CI: 20.4–1086.1, $P < 0.0001$) higher, respectively, in HIV-positive individuals than in HIV-negative individuals (Table III).

Among the 67 subjects who were born after 1984, the year that the universal HBV vaccination program was launched in Taiwan, the HBsAg-positive rate was 6%, significantly lower than among those born before 1984 (17.9%) (OR 0.31, 95% CI: 0.10–0.91, $P = 0.03$).

Over one-third of the heroin injection users (38.3%) had concomitant dual (HBV and HCV, HCV and HIV, or HBV and HDV), triple (HIV, HCV and HBV, or HCV, HBV, and HDV), or quartic (HIV, HCV, HBV, and HDV) viral infections, a rate which was significantly higher than in the other groups (4.9% for heroin smokers, 2% for methamphetamine users, and 3% for club drug users; $P < 0.0001$).

DISCUSSION

HIV infection spread rapidly during the period 2004 to 2007 in Taiwan, and injection drug usage was the leading route of HIV transmission [Centers for Disease Control Taiwan, 2003, 2005, 2007; Chen and Kou, 2007]. This study found that 6.9% (95% CI: 5.1–8.7) of illicit

TABLE I. Demographics of the Incarcerated Male Substance Users in Taiwan

Variable	Non-injection drug users, N = 561 (%)	Injection drug users, N = 192 (%)
Age, mean \pm SD years (range)	30.4 \pm 7.4 (16–57)	32.4 \pm 7.1 (19–55)
Employment status ^a		
Unemployed	67 (12.1)	15 (7.8)
Blue-collar	323 (58.5)	130 (67.7)
White-collar	45 (8.2)	9 (4.7)
Other	117 (21.2)	38 (19.8)
Years of education ^a (mean \pm SD)	10.5 \pm 2	10 \pm 2
≤ 9 years	251 (44.7)	87 (45.6)
> 9 years	310 (55.3)	104 (54.4)
Marital status ^a		
Unmarried	304 (55.3)	95 (49.2)
Married/cohabited	189 (34.4)	62 (32.3)
Divorced/separated	57 (10.4)	35 (18.5)
Risk factors for bloodborne or sexually transmitted infections ^b		
Previous blood transfusion	14 (16.0)	3 (9.1)
Multiple sexual partners	1 (1.1)	0 (0)
Nonconsistent condom usage	51 (57.9)	14 (42.5)
Prostitution	14 (15.9)	4 (12.1)
Shared injection equipment	0 (0)	7 (20.6) ^c
> 1 risk factors	14 (15.9)	4 (12.1)

Non-injection drug users: including users of club drugs, methamphetamine, and heroin non-injection.

^aMissing data excluded.

^b88 non-injection drug users and 33 injection drug users enrolled for face-to-face questionnaire.

^cOdds ratio 23.42 (95% CI: 2.67–530.30), $P = 0.00043$.

TABLE II. Prevalence of HIV, HBV, HCV, and HDV Among Incarcerated Male Substance Users in Taiwan

	Total	Non-injection drug users				Injection drug users	
		Club drug	Methamphetamine	Heroin		Subtotal	Heroin injection
					non-injection		
No.	753	99	356	106	561	192	
Anti-HCV-positive, % (95% CI)	30.5 (27.23–33.93)	3.0 (0.63–8.60)	8.1 (5.51–11.46)	24.5 (16.69–33.84)	10.3 (7.94–13.16)	89.6 ^b (84.37–93.52)	
Anti-HIV-positive, % (95% CI)	6.9 (5.19–8.95)	1.0 (0.03–5.50)	0.3 (0.01–1.55)	0.9 (0.02–5.14)	0.5 (0.11–1.55)	25.5 ^b (19.52–32.30)	
HBsAg-positive, % (95% CI)	16.9 (14.24–19.71)	17.2 (10.33–26.06)	17.1 (13.33–21.40)	16.0 (9.63–24.43)	16.9 (13.92–20.30)	16.7 (11.69–22.71)	
Anti-HDV-positive in HBsAg carriers ^a , % (95% CI)	13.7 (8.19–21.04)	0 (0–19.51)	6.7 (1.85–16.20)	6.25 (0.16–30.23)	5.3 (1.77–12.10)	38.7 ^b (21.85–57.81)	

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HIV, human immunodeficiency virus.

^a124 HBsAg-positive subjects had anti-HDV tested.^bLogistic regression analysis for injection drug users comparing with non-injection drug users, $P < 0.0001$.

drug users, and 25.5% (95% CI: 19.3–31.7) of injection drug users in a male detoxification center were HIV-positive; these rates were much higher than those reported in previous studies [Centers for Disease Control Taiwan, 2003; Chen and Kou, 2007]. By the year of 2003, the HIV infection rate among injection drug users was only 0.09% in Taiwan [Chen and Kou, 2007]. One of the possible explanations for this rising epidemic is the increase of smuggled illicit drugs, including heroin, into Taiwan since 2002 [Ministry of Justice Taiwan, 2005; Cheng et al., 2007]. In addition, previous study had demonstrated that sharing the needles and paraphernalia among injection drug users were important risk factors for getting HIV infection in Taiwan [Cheng et al., 2007].

Chronic liver disease has emerged as a leading cause of morbidity and mortality among persons living with HIV [Bonacini et al., 2004]. A study in the United States found that the prevalence of chronic HBV infection in the HIV-infected cohort was 7.6%, significantly higher than the 0.5–1% prevalence in the general population [Kellerman et al., 2003]. With a difference from western countries, HBV infection has been hyperendemic in Taiwan for decades, with reported natural infection rates in the range of 80–90%, and HBsAg carrier rates in the range of 15–20% among Taiwanese adults [Chen and Sung, 1978; Wu et al., 1980; Sung et al., 1984]. Vertical transmission from mother to child contributed the high prevalence of HBsAg carriage in the population [Stevens et al., 1975]. Infections in early childhood may be another cause of HBsAg carriage [Stevens et al., 1975]. In 1984, the Taiwan government launched a universal vaccination program for newborns; by the year 2005, the prevalence of chronic HBV carriers had dropped to 1.4% [Lu et al., 2006; Su et al., 2007]. In the present study, the HBsAg-positive rate was 17.9% among subjects born before the year 1984, a rate that is consistent with that among the general adult population in Taiwan. However, the HBsAg-positive rate was 6% in those born after the year 1984, which is significantly lower than the rate of 17.9% in those born before the year 1984, but is higher than the rate of 1.4% among general hepatitis B vaccination cohort. Based on the HBV serostatus of drug users born before 1984 in this study, we speculate that the mode of HBV transmission was perinatal infection or infection in their early childhood. For drug users born after 1984 who may not have been vaccinated during infancy, or in whom immunity may have waned with time after vaccination, parenteral transmission via injecting drug use is a possible route for HBV infection.

The HDV infection rate was previously estimated to be 2.7% among the HBsAg-positive population in Taiwan [Chung et al., 1988]. A study in 1990 in Taiwan found that the prevalence of HDV infection in HBsAg-positive injection drug users was 91% [Hsu et al., 1990]. In 1997, some investigators reported that the prevalence of HDV in HBsAg-positive injection drug users had decreased to 39%; however, the prevalence of HIV infection was still 0% at that time [Kao et al., 2002].

TABLE III. Associated Factors for HIV Infection Among Incarcerated Male Substance Users in Taiwan

	HIV status		Odds ratio ^b (95% CI)
	Positive, n = 52 (%)	Negative, n = 701 (%)	
Category of major drug uses			
Non-injection drug users	3 (5.8%)	558 (79.6%)	1 (0.00–0.05)
Club drug	1 (1.9%)	98 (14.0%)	
Methamphetamine	1 (1.9%)	355 (50.6%)	
Heroin, non-injection	1 (1.9%)	105 (15.0%)	
Heroin injectors	49 (94.2%)	143 (20.4%)	63.8 ^c (19.6–207.8)
Coinfections of viral hepatitis			
Anti-HCV-positive	51 (98.1%)	179 (25.5%)	149.0 ^c (20.4–1086.1)
HBsAg-positive	6 (11.5%)	121 (17.3%)	0.64 (0.21–1.51)
Anti-HDV-positive in HBsAg carriers ^a	1 (16.7%)	16 (13.2%)	1.28 (0.14–11.6)

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HIV, human immunodeficiency virus.

^a124 HBsAg-positive subjects had anti-HDV tested.

^bOdds ratios from logistic regression analysis.

^c $P < 0.0001$.

Similarly, a report published in 1997 demonstrated a decrease in HDV infection among high-risk populations in Taiwan, such as heterosexual prostitutes and their clients [Huo et al., 1997]. Our finding that 38.7% of HBsAg-positive injection drug users were superinfected with HDV is similar to the findings reported in the latter two studies. Whether the present HIV epidemic will contribute to a subsequent increase in HDV co-infection remains unclear and should be closely monitored.

Approximately one-fourth of HIV-positive patients in the USA are also infected with HCV [Rochstroh et al., 2005]. HIV/HCV co-infection rates exceeded 75% in HIV-positive persons who were infected parenterally [Rochstroh et al., 2005]. In Taiwan, 2–4% of the general population was infected with HCV in 2004 [Lai et al., 2004]. A study conducted before the start of the injection drug users-driven HIV epidemic in Taiwan reported that 59.5% of injection drug users were infected with HCV [Kao et al., 2002]. Other investigators reported that 12% of HIV-infected patients, mainly homosexual and heterosexual men, were coinfecting with HCV [Hung et al., 2005]. The prevalence rates for HCV infection and HIV/HCV coinfection were much higher in our study than those reported in previous studies. The major reason for HCV infection is injection drug usage, and tattooing [Ko et al., 1992; Lai et al., 2007] and having unprotected sex [Elifson et al., 2006; Cheng et al., 2007] might be the other causes. In this study, heroin non-injection group had significantly higher rate of HCV infection than methamphetamine group and club drug group. Since the subjects were classified according to the “major substances” used before incarceration, the group of heroin smokers might include those who injected heroin occasionally.

Multiple hepatitis virus infections were common among injection drug users in this study. However, patients with multiple hepatitis virus infections have often been excluded from randomized trials of hepatitis therapies [Gaeta et al., 2006]. Whether these individuals have more rapid deterioration of liver function

and higher morbidity and mortality warrants further investigation.

This study demonstrated that the introduction of HIV infection on the injection drug users since 2004 in Taiwan is associated with higher rates of HCV infection and HDV superinfection in HBV carriers than previous studies. It is reasonable to assume that an effective preventive strategy that targets HIV infection in injection drug users would be beneficial in the prevention of chronic viral hepatitis. At the end of 2005, the Taiwan government launched a harm-reduction program that included methadone maintenance therapy and a needle-exchange program. It was found that the incidence of newly diagnosed HIV cases had decreased by 13.5% at the end of 2006 and by 33.9% at the end of 2007 [Centers for Disease Control Taiwan, 2007]. Whether the HCV, HBV, and HDV infections showed the same decreases warrants close monitoring.

There are several limitations in this study. First, few of the subjects (10%) were born after 1984, the year that universal hepatitis B vaccination program was launched. The HBsAg-positive rate among these subjects was significantly lower than that among subjects born before 1984 (6% vs. 17.9%). It remains unclear whether individuals who had been vaccinated against HBV at birth or during childhood and engaged in behaviors with high risk for HIV transmission in adulthood benefited from the vaccination because vaccination records were not available in this study. Second, all of the recruited subjects in this study were prison inmates. Therefore, the results might not be representative of illicit drug users in the general population in Taiwan.

In conclusion, it was found that the rates of HIV, HCV, and HDV infections were significantly higher in heroin injection drug users than non-injection drug users; furthermore, HIV-positive drug users had increased odds for being heroin injectors and for having HCV co-infections. These comorbidities and their consequences among injection drug users and HIV-positive patients should be closely monitored.

ACKNOWLEDGMENTS

We wish to thank the Ministry of Justice and the Taoyuan Prison.

REFERENCES

- Aceijas C, Stimson GV, Hickman M, Rhodes T, United Nations Reference Group on HIV/AIDS Prevention and Care among IDU in Developing and Transitional Countries. 2004. Global overview of injecting drug use and HIV infection among injecting drug users. *AIDS* 18:2295–2303.
- Benhamou Y, Bochet M, Di Martino V, Charlotte F, Azria F, Coutellier A, Viduad M, Bricaire F, Opolon P, Katlama C, Poynard T. 1999. Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus co-infected patients. The Multivirc Group. *Hepatology* 30:1054–1058.
- Bica I, McGovern B, Dhar R, Stone D, McGowan K, Scheib R, Snyderman DR. 2001. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis* 32:492–497.
- Bonacini M, Louie S, Bzowej N, Wohl AR. 2004. Survival in patients with HIV infection and viral hepatitis B or C: A cohort study. *AIDS* 18:2039–2045.
- Borkowf CB. 2006. Constructing binominal confidence intervals with near nominal coverage by adding a single imaginary failure or success. *Statist Med* 25:3679–3695.
- Centers for Disease Control, Department of Health, Executive Yuan, Taiwan. 2003. Statistics of communicable diseases and surveillance reports in Taiwan area. Taipei: Centers for Disease Control, Department of Health, Executive Yuan, Taiwan.
- Centers for Disease Control, Department of Health, Executive Yuan, Taiwan. 2005. Statistics of communicable diseases and surveillance reports in Taiwan area. Taipei: Centers for Disease Control, Department of Health, Executive Yuan, Taiwan.
- Centers for Disease Control Department of Health, Executive Yuan, Taiwan. 2007. Statistics of communicable diseases and surveillance reports in Taiwan area. Taipei: Centers for Disease Control, Department of Health, Executive Yuan, Taiwan.
- Chen YM, Kou SH. 2007. HIV-1 in Taiwan. *Lancet* 369:623–625.
- Chen DS, Sung JL. 1978. Hepatitis B virus infection and chronic liver disease in Taiwan. *Acta Hepatogastroenterol* 25:423–430.
- Cheng SH, Chiang SC, Hsieh YL, Chang YY, Liu YR, Chu FY. 2007. Gender difference in the clinical and behavioral characteristics of Human Immunodeficiency Virus-infected injection drug users in Taiwan. *J Formos Med Assoc* 106:453–467.
- Chung DC, Ko YC, Chen CJ, Wu CC, Chen ER, Liaw YF, Hwang SJ. 1988. Seroepidemiological studies on hepatitis B and D viruses infection among five ethnic groups in southern Taiwan. *J Med Virol* 26:411–418.
- Colin JF, Cazals-Hatem D, Lioriot MA, Martinot-Peignoux M, Pham BN, Auferin A, Degott C, Benhamou JP, Erlinger S, Valla D, Marcellin P. 1999. Influence of human immunodeficiency virus infection on chronic hepatitis B in homosexual men. *Hepatology* 29:1306–1310.
- Elifson KW, Klein H, Sterk CE. 2006. Predictors of sexual risk-taking among new drug users. *J Sex Res* 43:318–327.
- Gaeta GB, Precone DF, Cozzi-Lepri A, Cicconi P, D'Arminio Monforte A. 2006. Multiple viral infections. *J Hepatol* 44:S108–S113.
- Hsu HM, Wang YF, Lo SH, Sun HC, Yip KK, Chen JS, Chuang CH, Chen DS. 1990. Hepatitis D virus infection among intravenous drug abusers in Taiwan: Analysis of risk factors and liver function tests. *J Med Virol* 31:76–81.
- Hung CC, Chen MY, Hsieh SM, Hsiao CF, Sheng WH, Chang SC. 2005. Impact of chronic hepatitis C infection on outcomes of patients with an advanced stage of HIV-1 infection in an area of low prevalence of co-infection. *Int J STD AIDS* 16:42–48.
- Huo TI, Wu JC, Lin RY, Sheng WY, Chang FY, Lee SD. 1997. Decreasing hepatitis D virus infection in Taiwan: An analysis of contributory factors. *J Gastroenterol Hepatol* 12:747–751.
- Jarlais Des DC, Semaan S. 2008. HIV prevention in injection drug users: 25 years and counting. *Psychosom Med* 70:606–611.
- Kao JH, Chen PJ, Lai MY, Chen DS. 2002. Hepatitis D virus genotypes in intravenous drug users in Taiwan: Decreasing prevalence and lack of correlation with hepatitis B virus genotypes. *J Clin Microbiol* 40:3047–3049.
- Kellerman SE, Hanson DL, McNaghten AD, Fleming PL. 2003. Prevalence of chronic hepatitis B and incidence of acute hepatitis B infection in human immunodeficiency virus-infected subjects. *J Infect Dis* 188:571–577.
- Ko YC, Ho MS, Chiang TA, Chang SJ, Chang PY. 1992. Tattooing as a risk of hepatitis C virus infection. *J Med Virol* 38:288–291.
- Kral AH, Bluthenthal RN, Lorvick J, Gee L, Bacchetti P, Edlin PR. 2001. Sexual transmission of HIV-1 among injecting drug users in San Francisco, USA: Risk factor analysis. *Lancet* 357:1397–1401.
- Lai SW, Ng KC, Li CI. 2004. Descriptive analysis of HBsAg and HCV antibody prevalence in patients receiving health check-ups: A hospital-based study. *Mid Taiwan J Med* 9:S64–S69 [In Chinese].
- Lai SW, Chang WL, Peng CY, Liao KF. 2007. Viral hepatitis among male amphetamine-inhaling abusers. *Intern Med J* 37:472–477.
- Lu SN, Chen CH, Chen TM, Lee PL, Wang JH, Tung HD, Hung CH, Lee CM, Changchien CH. 2006. Hepatitis B virus infection in adolescents in a rural township—15 years subsequent to mass hepatitis B vaccination in Taiwan. *Vaccine* 24:759–765.
- Ministry of Justice, Executive Yuan, Taiwan. 2005. Justice Statistics. Available from <http://www.moj.gov.tw>, Accessed March 27, 2006.
- Nelson KE, Galai N, Safaeian M, Strathdee SA, Celentano DD, Vlahov D. 2002. Temporal trends in the incidence of Human Immunodeficiency Virus Infection and risk behavior among injection drug users in Baltimore, Maryland, 1988–1998. *Am J Epidemiol* 156: 641–653.
- Rochstroh J, Mocroft A, Soriano V, Tural C, Losso MH, Horban A, Kirk O, Phillips A, Lederberger B, Lundgren JD. The EuroSIDA study group. 2005. Influence of hepatitis C on HIV disease progression and response to highly active antiretroviral therapy. *J Infect Dis* 192:992–1002.
- Rosengard C, Anderson B, Stein MD. 2004. Intravenous drug users' HIV-risk behaviors with primary/other partners. *Am J Drug Alcohol Abuse* 30:225–236.
- Stevens CE, Beasley RP, Tsui J, Lee WC. 1975. Vertical transmission of hepatitis B antigen in Taiwan. *N Eng J Med* 292:771–774.
- Su FH, Chen JD, Cheng SH, Lin CH, Liu YH, Chu FY. 2007. Seroprevalence of hepatitis-B infection amongst Taiwanese university students 18 years following the commencement of a national hepatitis-B vaccination program. *J Med Virol* 79:128–143.
- Sung JL, Chen DS, Lai MY, Yu JY, Wang TH, Wang CY, Yu JY, Lee CY. 1984. Epidemiological study of hepatitis B virus infection in Taiwan. *Chin J Gastroenterol* 1:1–9.
- UNAIDS. 2003. AIDS epidemic update. Geneva: UNAIDS.
- UNAIDS. 2004. Report on the global HIV/AIDS epidemic. Geneva: UNAIDS.
- UNAIDS. 2005. Reports on the global HIV/AIDS epidemic. Geneva: UNAIDS.
- Wu JS, Chen CH, Chiang YH, Lee YC, Lee MH, Ko YC, Hu HT. 1980. Hepatitis B virus infection in Taiwan with reference to anti-HBc versus HBsAg and anti-HBs. *J Formosan Med Assoc* 79:760–767.