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## REVIEW ARTICLE

# Epidemiology of sexually transmitted viral hepatitis in human immunodeficiency virus-positive men who have sex with men in Asia



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Both human immunodeficiency virus (HIV) and viral hepatitis constitute major disease burden globally. As with other parts of the world, the HIV epidemic in Asia impacts mainly on men who have sex with men, one of the at-risk populations for sexually transmitted viral hepatitis. With the increasing availability of effective antiretroviral therapy, HIV-related mortality of people living with HIV has markedly reduced. Liver disease has become an important cause of mortality and morbidity in the HIV-infected population. With the improvement of socioeconomic conditions and availability of healthcare in Asian countries in recent years, the epidemiology of sexually transmitted viral hepatitis among HIV-positive men who have sex with men has also evolved. This review updates the epidemiology of different types of sexually transmitted viral hepatitis in this defined population in Asia.

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## Introduction

Globally, approximately 1.4 million people die from viral hepatitis annually.<sup>1</sup> Although these infections may be transmitted through various routes, many types of viral hepatitis are transmissible by sexual contact. This is especially true in defined at-risk populations such as men who have sex with men (MSM). Outbreaks of sexually transmitted hepatitis A among MSM has been extensively reported in Western countries,<sup>2–4</sup> whereas hepatitis C has emerged as a commonly encountered sexually transmitted infection among MSM in the past decade, especially among individuals with human immunodeficiency virus (HIV)-positive MSM.<sup>5,6</sup>

The highest burden of the HIV epidemic in Asia, apart from the injecting drug-using population in Central Asia, lies on the MSM population and is spread through sexual transmission.<sup>7,8</sup> With the increasing availability of effective combination antiretroviral therapy, the mortality and morbidity of people living with HIV has markedly decreased.<sup>9</sup> However, chronic liver disease has become an important cause of mortality in the HIV-infected population, a significant proportion of which is related to hepatitis B and C.<sup>10,11</sup>

In this article, we review the epidemiology of sexually transmitted viral hepatitis, including hepatitis A, B, C, and D in the Asian HIV-positive MSM population. In addition, we explore the emerging role of other agents, such as hepatitis E virus (HEV), in contributing to sexually transmitted liver diseases in endemic settings. Studies in English were identified by PubMed using the keywords “HIV,” “hepatitis,” and “MSM,” and supplemented with references of relevant publications.

## Epidemiology of hepatitis A in HIV-positive MSM in Asia

The endemicity of hepatitis A in Asia is widely variable, ranging from areas of low (e.g., Japan, Singapore) and intermediate endemicity (e.g., Hong Kong) to high endemicity (e.g., India).<sup>12–14</sup> Hepatitis A virus (HAV) seroprevalence among general adult populations in Asia ranges from 25.9% to 92.6%.<sup>12,15–19</sup> Owing to the rise in sanitation standards, the endemicity of hepatitis A in many developing Asian countries has been decreasing over the past 2 decades. Paradoxically, in such transitional areas without mass vaccination programs, increasing populations are at risk of hepatitis A, who have not contracted it as an asymptomatic infection during childhood; this is reflected by the outbreaks of HAV reported in Japan, Thailand, Korea, and Singapore.<sup>16,20–22</sup>

The HAV seroprevalence among HIV-positive MSM in Asian countries is summarized in [Table 1](#). The reported HAV seroprevalence ranged from 15.1% to 50.5%<sup>23–28</sup> and, like in the general population, was found to be associated with increasing age.<sup>23,27</sup> The overall prevalence was higher than that reported in the United States (16.1%)<sup>29</sup> but rather comparable to that in Greece (35%).<sup>30</sup> Although the reported seroprevalence rates among HIV-positive MSM seem to be lower than in the general Asian adult population, it should be noted that most seroprevalence figures among

HIV-positive MSM are reported from resource-rich settings in Asia, and from relatively young individuals who were mostly aged < 50 years old.

Whereas outbreaks of HAV among HIV-positive MSM are reported in Europe,<sup>31,32</sup> they are rarely reported in Asian countries. An outbreak involving 13 HIV-positive MSM was reported in Japan in 1999.<sup>33</sup> The majority (92%) of the infected individuals was coinfecting with syphilis, and some (38.5%) had amebiasis. Although all patients recovered from acute hepatitis A, antiretroviral therapy was interrupted because of infection in a proportion (37.5%) of patients.

Overall, with the changing endemicity of hepatitis A in the region, a significant proportion of HIV-positive MSM, especially young MSM who are sexually active and from developed countries in Asia, are susceptible to the infection.<sup>34</sup> Although reports of HAV outbreaks among Asian HIV-positive MSM have been scarce so far, we need to remain vigilant, given their susceptibility as well as the potential connectivity from the sexual affiliation networking in this at-risk population.<sup>35</sup> Despite the reduced immunogenicity of hepatitis A vaccine compared with HIV-uninfected adults, immunization remains one important way to prevent hepatitis A among HIV-positive MSM. Although the extra benefit for the use of an additional dose of hepatitis A vaccine in HIV-infected adults remains uncertain, studies have demonstrated durable seropositive responses among HIV-infected adults with suppressed HIV viral load and high CD4 counts.<sup>36–38</sup>

## Epidemiology of hepatitis B in HIV-positive MSM in Asia

Asia has the highest burden of hepatitis B infection in the world.<sup>39</sup> With the commitment of the World Health Organization Western Pacific Region Office and member countries for hepatitis B control through a childhood immunization program, the hepatitis B surface antigen (HBsAg) seroprevalence in children at least 5 years of age in some Asian countries has reached the target of <2%.<sup>40</sup> However, the disease burden of chronic hepatitis B among the adult population remains intermediate to high in the region, with HBsAg seroprevalence up to >8% in the adult population.<sup>39</sup>

The HBsAg seroprevalence of HIV-positive MSM in Asia is summarized in [Table 1](#).<sup>23–27,41–46</sup> It is not surprising that the HBsAg seroprevalence among HIV-positive MSM is at least comparable, if not higher, than in the general adult population, given the similar route of transmission for both infections. In regions with territory-wide universal neonatal hepatitis B virus (HBV) immunization programs (e.g., Taiwan and Hong Kong), there is limited data showing that the burden of chronic hepatitis B among HIV-positive MSM might be on a decreasing trend over the past decade. In Taiwan, HBsAg seroprevalence among HIV-positive MSM born prior to and after the implementation of the universal neonatal HBV immunization program in 1986 was 7.8% and 3.7%, respectively.<sup>41</sup> In Hong Kong, where the universal neonatal HBV immunization program was implemented in 1988, HBsAg seroprevalence among HIV-positive MSM in the

**Table 1** Studies on seroprevalence/incidence of hepatitis A, B, C, and D in HIV-positive MSM in Asia.

References	Location	Period of study	Number tested	Seroprevalence (%)	Incidence of infection	Remarks
<i>Hepatitis A</i>						
Lam et al [23]	Hong Kong	2007–2013	1207	Anti-HAV: 37.1	—	Seroprevalence associated with increasing age
Tseng et al [24]	Taiwan	2009–2010	438	Anti-HAV: 15.1	—	
Lee et al [25]	Southern Taiwan	2000–2005	75	Anti-HAV: 40	—	
Sun et al [26]	Taiwan	2004–2007	658	Anti-HAV: 50.5	—	Seroprevalence associated with increasing age
Linkins et al [27]	Bangkok	2006–2008	290	Anti-HAV: 32.4	—	
Baek et al [28]	Korea	2008–2010	77	Anti-HAV: 37.3	—	
<i>Hepatitis B</i>						
Lam et al [23]	Hong Kong	2000–2013	1273	HBsAg: 9.6 Anti-HBs: 54.3	—	HBsAg seropositivity associated with syphilis and anti-HCV+
Sun et al [41]	Taiwan	2006–2012	776 <sup>a</sup>	HBsAg: 7.8 Anti-HBc: 30.3 HBsAg: 3.7 Anti-HBc: 26.3	HBsAg seroconversion: 0.486/100 py ( <i>n</i> = 479)	
Tseng et al [24]	Taiwan	2009–2010	438	HBsAg: 16.4	—	
Lee et al [42]	Southern Taiwan	1997–2010	16	HBsAg: 6.3	—	
Lee et al [25]	Southern Taiwan	2000–2005	113	HBsAg: 17.7	—	
Sun et al [26]	Taiwan	2004–2007	658	HBsAg: 20.5	—	
Fukisaki et al [46]	Japan	2003–2007	394	HBsAg: 7.9	—	
Chow et al [43]	China	2000–2013	151	HBsAg: 18.3	—	
Heng et al [44]	Singapore	1990–1992	47	HBsAg: 8.5	—	
Linkins et al [27]	Bangkok	2006–2008	290 (46.8% MSM)	Anti-HBc: 46.8 HBsAg: 15.8 Without any positive HBV marker positive: 22.4 HBsAg: 13.4	—	
Zaw et al [45]	Myanmar	2005–2012	176	HBsAg: 13.4	—	
<i>Hepatitis C</i>						
Lam et al [23]	Hong Kong	2000–2013	1272	Anti-HCV: 1.3	—	Associated with higher education and history of STIs
Lin et al [67]	Hong Kong	1998–2013	1311	—	Overall 2.2/1000 py 1998–2002: 1.3/1000 py 2002–2007: 1.9/1000 py 2007–2013: 4.7/1000 py	
Sun et al [41]	Taiwan	2006–2012	752	Anti-HCV: 3.7	—	
Tseng et al [24]	Taiwan	2009–2010	438	Anti-HCV: 5.5	—	Associated with syphilis
Lee et al [25]	Southern Taiwan	2000–2005	113	Anti-HCV: 5.3	—	
Sun et al [26]	Taiwan	2004–2007	658	Anti-HCV: 6.4	—	
Lee et al [42]	Southern Taiwan	1997–2010	16	Anti-HCV: 6.1	—	Associated with syphilis
Sun et al [41]	Taiwan	1994–2010	892 (81.9% MSM, none IDU)	—	Overall 7/1000 py 1994–2000: 0/1000 py 2001–2005: 2.3/1000 py 2006–2010: 10.1/1000 py	
Nishijima et al [68]	Japan	2005–2012	753 (19% IDU)	—	Overall 9.35/1000 py 2005–2006: 0/1000 py 2007–2008: 3/1000 py 2009–2010: 7.7/1000 py 2011–2012: 24.9/1000 py	

Table 1 (continued)

References	Location	Period of study	Number tested	Seroprevalence (%)	Incidence of infection	Remarks
Chow et al [43]	China	2000–2013	363	Anti-HCV: 8.4	—	
Zhang et al [76]	Beijing, China	2005–2006	16	Anti-HCV: 18.8	—	% of IDU not well described
An et al [77]	China	NA	513	Anti-HCV: 1.94	—	
Zhao et al [78]	Shandong, China	2000–2010	230	Anti-HCV: 24.3	—	Associated with syphilis; % of IDU not well described
Lim et al [79]	Singapore	2006–2011	739 (33.7% MSM)	Anti-HCV: 2	—	
Zaw et al [45]	Myanmar	2005–2012	176	Anti-HCV: 3.4	—	
Hung et al [85]	Taiwan	1992–2012	257	Anti-HDV: 7.4	Overall 9.07/1000 py <sup>b</sup> 1992–2001: 0/1000 py 2002–2006: 3.91/1000 py 2007–2012: 13.6/1000 py	Associated with elevated RPR
Lee et al [86]	Southern Taiwan	2009–2012	51	Anti-HDV: 7.8	—	
Liu et al [87]	Taiwan	2011	1371	Anti-HEV: 6.3		

HAV = hepatitis A virus; HBSAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HDV = hepatitis D virus; HEV = hepatitis E virus; HIV = human immunodeficiency virus; IDU = injecting drug users; MSM = men who have sex with men; py = person-years; NA = not applicable; RPR = rapid plasma reagin; STI = sexually transmitted infection.

<sup>a</sup> Among the 776 patients, 244 were born before 1986, 532 were born after 1986.

<sup>b</sup> Among a total of 375 patients.

largest HIV clinic was 12.3%, 10.1%, and 8.3% in the period 2000–2004, 2005–2009, and 2010–2013, respectively.

Compared with those who acquired HIV via the heterosexual route, HIV-positive MSM seemed to have higher prevalence of hepatitis B. Most studies, which also include the data of those who acquired HIV via the heterosexual route, showed a higher proportion of HIV-positive MSM with positive HBV markers compared with HIV-positive heterosexuals. A study from Singapore showed that 72.7% HIV-positive MSM versus 48% HIV-positive heterosexuals tested positive for HBV markers (HBsAg and/or anti-HBs and/or Hepatitis B core antibody (anti-HBc)).<sup>44</sup> A Taiwanese study found that HBsAg prevalence among HIV-positive MSM and heterosexuals was 17.7% and 12.8%, respectively,<sup>24</sup> whereas another study from Myanmar showed HBsAg seroprevalence of 13.4% and 9%, respectively.<sup>45</sup> However, a report from Hong Kong showed a higher HBsAg seroprevalence among HIV-positive heterosexual males (12.1%) than MSM (9.6%), probably owing to the younger age in the latter group.<sup>23</sup>

Data regarding the HBV genotype among HIV-positive MSM in Asia are limited. Similar to the majority of the Asian hepatitis B carrying general population,<sup>47</sup> HBV genotypes B and C are the most commonly found genotypes in the HIV-infected population in Taiwan.<sup>48</sup> However, studies from Japan showed that genotype A, the predominant genotype among MSM in Europe, might be more commonly found among HIV-positive MSM. In 2001, genotype A was reported as predominantly found in HIV-positive MSM, in contrast to other genotypes found among HIV-positive heterosexual or hemophilic patients.<sup>49</sup> More recent data also showed that

genotype A was the major circulating HBV genotype among HIV-positive MSM in Japan.<sup>46</sup> The predominant HBV genotype among HIV-positive MSM in other Asian countries is unknown.

Not surprisingly, the burden of HIV–HBV coinfection among MSM in Asia is significant. Despite limited data on decreasing trend of HBsAg seropositivity in HIV-positive MSM in regions with the universal neonatal HBV immunization program, the impact on the overall epidemiology of HIV–HBV coinfection among MSM in Asia is still uncertain. Moreover, serological markers for HBV are associated with host immunity and viral activities.<sup>50</sup> Thus, screening for HBV infection and recommendations on vaccination, especially with the use of increased dose to enhance serological response,<sup>51,52</sup> for HBV susceptible HIV-positive MSM remains important. Furthermore, the use of antiretroviral therapy might also influence the epidemiology of hepatitis B in HIV-positive MSM. In a study reported from Taiwan, none of the 133 HIV-positive MSM on antiretroviral therapy with lamivudine and/or tenofovir developed HBsAg seroconversion during a follow-up period up to 6 years.<sup>41</sup> Another two studies from Taiwan also found a lower incidence of HBV infection among those who were on lamivudine- or tenofovir-containing regimen.<sup>53,54</sup>

### Epidemiology of hepatitis C in HIV-positive MSM in Asia

Hepatitis C virus (HCV) has emerged as a sexually transmitted infection among HIV-positive MSM in the West. Since

2000, outbreaks of HCV among HIV-positive MSM who denied injecting drug use have been reported from the United States,<sup>55,56</sup> Europe,<sup>57,58</sup> and Australia.<sup>59</sup> The HCV incidence in HIV-positive MSM increased from 1 to 3/1000 patient-years (py) in the late 1990s to >10/1000 py from the early 2000s onward.<sup>60</sup> Certain risk factors associated with infection identified included unsafe sex, fisting, and sexually transmitted infections.<sup>61–65</sup>

A similar trend has also been reported in Asia recently. In 2012, a Taiwanese study described an increasing incidence of hepatitis C in HIV-infected patients, and among them >80% were MSM.<sup>66</sup> Similar findings were reported from Hong Kong and Japan.<sup>67,68</sup> All of them showed a rise in the incidence of hepatitis C among HIV-positive MSM in the past decade. Moreover, syphilis was found to be an independent factor associated with incident hepatitis C in Taiwan and Hong Kong, and higher education level was another independent factor found in the study from Hong Kong.<sup>67</sup> These reporting of HCV as a sexually transmitted infection among HIV-positive MSM in these resource-rich settings in Asia echoed the changing epidemiology of hepatitis C in Western countries where improved survival and serosorting were proposed to be contributing factors for the increasing prevalence of sexually transmitted infections including HCV.<sup>69</sup> The survival of people living with HIV has improved with the accessibility of antiretroviral therapy and good medical care in Asia, especially in resource-rich settings.<sup>9,70</sup> However, the practice of serosorting among HIV-positive MSM, which is well recognized in Western countries, is largely unknown in Asia. Only one study from Taiwan reported that 27% of HIV-positive MSM under medical care practiced serosorting.<sup>71</sup>

HCV genotypes 1a and 4d are the predominant genotypes in sexually transmitted HCV in HIV-positive MSM in Europe, and there is robust evidence on MSM-specific clustering.<sup>60,72,73</sup> Genotype 1a predominates in HIV-positive MSM in the United States, but there is a lack of information on clustering.<sup>74</sup> Genotype 3a is more prevalent among Australian HIV-positive MSM, however, around one half of the acute HCV infections among HIV-positive MSM in Australia were attributed to injecting drug use instead of sexual transmission.<sup>59</sup> In Asia, limited data found evidence of transmission clusters among HIV-positive MSM, but with different genotypes compared with those found in Western countries. In the Taiwanese study, the phylogenetic analysis revealed seven HCV transmission clusters or pairs (4 within genotype 1b, 2 within genotype 2a, and 1 within genotype 3a),<sup>66</sup> and a monophyletic cluster of HCV-3a lineage was found among HIV-positive MSM in Hong Kong.<sup>75</sup>

Although incident HCV has been increasingly reported, the anti-HCV seroprevalence rates among HIV-positive MSM in most Asian countries were <10% (Table 1).<sup>23–27,41–45,67,68,76–79</sup> Two studies from China reported an exceptionally high anti-HCV seroprevalence of 18.8% and 24.3%, however, the injecting drug use in these studies was not well described.<sup>76,78</sup>

### Epidemiology of hepatitis D in HIV-positive MSM in Asia

Hepatitis D virus (HDV) requires the presence of HBV to cause infection in humans, and is mainly transmitted

through parenteral and sexual routes.<sup>80</sup> In the early 1990s, heterosexual exposure was found to be an effective route of transmission of HDV in the general population.<sup>81,82</sup> Among the HIV-infected population, HDV infection occurred mainly among injecting drug users.<sup>83,84</sup> Studies on the seroprevalence of anti-HDV among HIV-positive MSM are limited. Two recent studies from Taiwan reported the anti-HDV seroprevalence to be 7.4% and 7.8% among HIV-positive MSM,<sup>85,86</sup> which was higher than the 3.2% rate reported in Europe.<sup>70</sup> In these two studies, the anti-HDV seroprevalence among HIV-positive injecting drug users was 44% and 25%, respectively. One of these studies revealed a significant increase in the incidence of HDV infection in the study cohort from 2007 onward. Moreover, recent HDV infection was found to be associated with elevated rapid plasma reagin titers.<sup>85</sup>

### Epidemiology of hepatitis E in HIV-positive MSM in Asia

Little is known about the epidemiology of hepatitis E among Asian HIV-positive MSM. Data from Taiwan indicate a seroprevalence of 6.3% and 4.0% among HIV-infected and HIV-uninfected MSM, respectively.<sup>87</sup> In the Asian setting, hepatitis E epidemiology has two faces. It remains a water-borne disease with person-to-person transmission in most parts of South and Southeast Asia; in these regions, MSM are at risk of direct acquisition of hepatitis E through practices such as oroanal sex. However, in industrialized Asian countries such as Japan, hepatitis E usually manifests as sporadic autochthonous infection caused by the consumption of meat derived from an increasing range of animal reservoirs of HEV.<sup>88,89</sup> Whereas fecal–oral human-to-human transmission of such autochthonous hepatitis E is generally considered to be limited, it is notable that MSM were found to be at an increased risk of acquiring hepatitis E irrespective of their HIV status in the United Kingdom, a region where hepatitis E is autochthonous and foodborne.<sup>90</sup>

Further studies are required to assess the epidemiology of hepatitis E in the Asian MSM population. This is particularly important, as there is evidence to suggest that HEV superinfection in Asian hepatitis B carriers tends to produce clinically severe liver disease,<sup>91</sup> a feature of relevance to the MSM population at risk of hepatitis B acquisition. Furthermore, HIV-positive patients with low CD4 counts stand a low, but well-defined, risk of chronic hepatitis E carriage with progression to liver cirrhosis.<sup>92</sup> Therefore, hepatitis E is likely to be a condition of emerging importance in the HIV-positive MSM population. Studies on the efficacy of the recently developed hepatitis E vaccine<sup>93,94</sup> suggest that it may be useful in prevention of hepatitis E among healthy MSM; however, the efficacy of the vaccine among HIV-infected MSM remains to be elucidated.

### Conclusion

Asian countries are diverse in terms of socioeconomic conditions and availability of healthcare. In resource-rich settings, the epidemiology of sexually transmitted viral hepatitis in HIV-positive MSM parallels the evolution of the

situation in developed countries in other parts of the world. However, there are also unique features in the disease burden and molecular epidemiology of sexually transmitted viral hepatitis in Asia. Overall, viral hepatitis is increasingly recognized as a sexually transmitted infection among Asian HIV-positive MSM. Enhanced surveillance and targeted prevention of viral hepatitis including improved sanitation and food safety, safer sex, and vaccination is becoming increasingly essential in HIV care in this part of the world.

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## References

- World Health Organization. Viral hepatitis. Available at: <http://www.who.int/hiv/topics/hepatitis/hepatitisinfo/en/>. [Accessed 26 Jan 2015].
- Christenson B, Broström C, Böttiger M, Hermanson J, Weiland O, Ryd G, et al. An epidemic outbreak of hepatitis A among homosexual men in Stockholm. Hepatitis A, a special hazard for the male homosexual subpopulation in Sweden. *Am J Epidemiol* 1982;116:599–607.
- Høybye G, Skinhøj P, Hentzer B, et al. An epidemic of acute viral hepatitis in male homosexuals. Etiology and clinical characteristics. *Scand J Infect Dis* 1980;12:241–4.
- Stene-Johansen K, Tjon G, Schreier E, et al. Molecular epidemiological studies show that hepatitis A virus is endemic among active homosexual men in Europe. *J Med Virol* 2007;79:356–65.
- Centers for Disease Control and Prevention. Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men—New York City, 2005–2010. *Morb Mortal Wkly Rep* 2011;60:945–50.
- Bottieau E, Apers L, Van Esbroeck M, et al. Hepatitis C virus infection in HIV-infected men who have sex with men: sustained rising incidence in Antwerp, Belgium, 2001–2009. *Euro Surveill* 2010;15:19673.
- Beyrer C, Abdool Karim Q. The changing epidemiology of HIV in 2013. *Curr Opin HIV AIDS* 2013;8:306–10.
- Huang YF, Chen CH, Chang FY. The emerging HIV epidemic among men who have sex with men in Taiwan. *J Formos Med Assoc* 2013;112:369–71.
- Wong KH, Chan KC, Lee SS. Delayed progression to death and to AIDS in a Hong Kong cohort of patients with advanced HIV disease during the era of highly active antiretroviral therapy. *Clin Infect Dis* 2004;39:853–60.
- Acharya C, Dharel N, Sterling RK. Chronic liver disease in the human immunodeficiency virus patient. *Clin Liver Dis* 2015;19:1–22.
- Rosenthal E, Roussillon C, Salmon-Céron D, et al. Liver-related deaths in HIV-infected patients between 1995 and 2010 in France: the Mortavic 2010 study in collaboration with the Agence Nationale de Recherche sur le SIDA (ANRS) EN 20 Mortalité 2010 survey. *HIV Med* 2015;16:230–9.
- Saha SK, Saha S, Shakur S, et al. Community-based cross-sectional seroprevalence study of hepatitis A in Bangladesh. *World J Gastroenterol* 2009;15:4932–7.
- Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. *Vaccine* 2010;28:6653–7.
- World Health Organization. Hepatitis A Vaccine. Available at [http://www.who.int/immunization/wer7505Hepatitis%20A\\_Feb00\\_position\\_paper.pdf?ua=1](http://www.who.int/immunization/wer7505Hepatitis%20A_Feb00_position_paper.pdf?ua=1). [Accessed 26 Jan 2015].
- Zhu Y, Yuan Z, Zhao Q, et al. Seroprevalence of hepatitis A virus antibody in a population aged 0–30 years in Shanghai, China: implications for hepatitis A immunization. *Epidemiol Infect* 2013;141:556–62.
- Lee SH, Kim HS, Park KO, et al. Prevalence of IgG anti-HAV in patients with chronic hepatitis B and in the general healthy population in Korea. *Korean J Hepatol* 2010;16:362–8.
- Rianthavorn P, Fakthongyoo A, Yamsut S, et al. Seroprevalence of hepatitis A among Thai population residing near Myanmar border. *J Health Popul Nutr* 2011;29:174–7.
- Lee HC, Ang LW, Chiew PK, et al. Changing epidemiological patterns of hepatitis A infection in Singapore. *Ann Acad Med Singapore* 2011;40:439–47.
- Kotwal A, Singh H, Verma AK, et al. A study of hepatitis A and E virus seropositivity profile amongst young healthy adults in India. *Med J Armed Forces India* 2014;70:225–9.
- Ishii K, Kiyohara T, Yoshizaki S, et al. Epidemiological and genetic analyses of a diffuse outbreak of hepatitis A in Japan, 2010. *J Clin Virol* 2012;53:219–24.
- Shim JJ, Chin SO, Lee CK, et al. Epidemiological changes in hepatitis A in Korea: increasing age and its effect on clinical outcomes. *Epidemiol Infect* 2012;140:2182–9.
- Poovorawan K, Chattakul P, Chattakul S, et al. The important role of early diagnosis and preventive management during a large-scale outbreak of hepatitis A in Thailand. *Pathog Glob Health* 2013;107:367–72.
- Lam P, Chan WK, Lin AW, et al. Surveillance of Viral Hepatitis in Hong Kong — 2013 Update Report. Department of Health, Hong Kong SAR. Available at <http://www.info.gov.hk/hepatitis/doc/hepsurv13.pdf>. [Accessed 26 Jan 2015].
- Tseng YT, Sun HY, Chang SY, et al. Seroprevalence of hepatitis virus infection in men who have sex with men aged 18–40 years in Taiwan. *J Formos Med Assoc* 2012;111:431–8.
- Lee HC, Ko NY, Lee NY, et al. Seroprevalence of viral hepatitis and sexually transmitted disease among adults with recently diagnosed HIV infection in Southern Taiwan, 2000–2005: upsurge in hepatitis C virus infections among injection drug users. *J Formos Med Assoc* 2008;107:404–11.
- Sun H, Kung HC, Ho YC, et al. Seroprevalence of hepatitis A virus infection in persons with HIV infection in Taiwan: implications for hepatitis A vaccination. *Int J Infect Dis* 2009;13:e199–205.
- Linkins RW, Chonwattana W, Holtz TH, et al. Hepatitis A and hepatitis B infection prevalence and associated risk factors in men who have sex with men, Bangkok, 2006–2008. *J Med Virol* 2013;85:1499–505.
- Baek JH, Kim CO, Park JY, et al. Clinical factors associated with hepatitis A virus seropositivity in HIV-infected adults living in a country with an epidemiologic shift for hepatitis A virus infection. *J Korean Med Sci* 2012;27:969–71.
- Hoover KW, Butler M, Workowski KA, et al. Low rates of hepatitis screening and vaccination of HIV-infected MSM in HIV clinics. *Sex Transm Dis* 2012;39:349–53.
- Kourkounti S, Pappas V, Leouo K, et al. Prevalence and titre of antibodies against Hepatitis A virus in HIV-infected men having sex with men in Greece. *Infez Med* 2014;22:206–12.
- Bordi L, Rozera G, Scognamiglio P, et al. Monophyletic outbreak of Hepatitis A involving HIV-infected men who have sex with men, Rome, Italy 2008–2009. *J Clin Virol* 2012;54:26–9.
- Dabrowska MM, Nazzal K, Wiercinska-Drapalo A. Hepatitis A and hepatitis A virus/HIV coinfection in men who have sex with men, Warsaw, Poland, September 2008 to September 2009. *Euro Surveill* 2011;16:1–4.

33. Ishida T, Nakamura T, Ajisawa A, et al. Outbreak of hepatitis A virus infection among HIV-1 seropositive men who had sex with men. *Jpn J Infect Dis* 1999;52:131–2.
34. Chan PC. Reemerging threat of hepatitis A among men who have sex with men in Taiwan. *J Formos Med Assoc* 2014;113:985–6.
35. Leung KK, Poon CM, Lee SS. A comparative analysis of behaviors and sexual affiliation networks among men who have sex with men in Hong Kong. *Arch Sex Behav* 2015;44:2067–76.
36. O1 Launay, Grabar S, Gordien E, et al. Immunological efficacy of a three-dose schedule of hepatitis A vaccine in HIV-infected adults: HEPAVAC study. *J Acquir Immune Defic Syndr* 2008;49:272–5.
37. Crum-Cianflone NF, Wilkins K, Lee AW, et al. Long-term durability of immune responses after hepatitis A vaccination among HIV-infected adults. *J Infect Dis* 2011;203:1815–23.
38. Tseng YT, Chang SY, Liu WC, et al. Comparative effectiveness of two doses versus three doses of hepatitis A vaccine in human immunodeficiency virus-infected and -uninfected men who have sex with men. *Hepatology* 2013;57:1734–41.
39. Hennessey K, Mendoza-Aldana J, Bayutas B, et al. Hepatitis B control in the World Health Organization's Western Pacific Region: targets, strategies, status. *Vaccine* 2013;31:J85–92.
40. World Health Organization. Hepatitis B control by 2012 in the WHO Western Pacific Region: rationale and implications. Available at <http://www.who.int/bulletin/volumes/87/9/08-059220/en/>. [Accessed 26 Jan 2015].
41. Sun HY, Cheng CY, Lee NY, et al. Seroprevalence of hepatitis B virus among adults at high risk for HIV transmission two decades after implementation of nationwide hepatitis B virus vaccination program in Taiwan. *PLoS One* 2014;9:e90194.
42. Lee KH, Ho TS, Shen CF, et al. Clinical and laboratory characteristics of human immunodeficiency virus-infected adolescents: experience from a single medical center. *J Microbiol Immunol Infect* 2012;45:329–36.
43. Chow EP, Tucker JD, Wong FY, et al. Disparities and risks of sexually transmissible infections among men who have sex with men in China: a meta-analysis and data synthesis. *PLoS One* 2014;9:e89959.
44. Heng BH, Goh KT, Chan R, et al. Prevalence of hepatitis B virus (HBV) infection in Singapore men with sexually transmitted diseases and HIV infection: role of sexual transmission in a city state with intermediate HBV endemicity. *J Epidemiol Community Health* 1995;49:309–13.
45. Zaw SK, Tun ST, Thida A, et al. Prevalence of hepatitis C and B virus among patients infected with HIV: a cross-sectional analysis of a large HIV care programme in Myanmar. *Trop Doct* 2013;43:113–5.
46. Fujisaki S, Yokomaku Y, Shiino T, et al. Outbreak of infections by hepatitis B virus genotype A and transmission of genetic drug resistance in patients coinfecting with HIV-1 in Japan. *J Clin Microbiol* 2011;49:1017–24.
47. Lin CL, Kao JH. Hepatitis B viral factors and treatment responses in chronic hepatitis B. *J Formos Med Assoc* 2013;112:302–11.
48. Sheng WH, Hung CC, Chang SY, et al. Differential clinical and virologic impact of hepatitis B virus genotypes B and C on HIV-coinfected patients receiving lamivudine-containing highly active antiretroviral therapy. *Clin Infect Dis* 2012;54:548–55.
49. Koibuchi T, Hitani A, Nakamura T, et al. Predominance of genotype A HBV in an HBV–HIV-1 dually positive population compared with an HIV-1-negative counterpart in Japan. *J Med Virol* 2001;64:435–40.
50. Sheng WH, Kao JH, Chen PJ, et al. Evolution of Hepatitis B serological markers in HIV-infected patients receiving antiretroviral therapy. *Clin Infect Dis* 2007;45:1221–9.
51. Ni JD, Xiong YZ, Wang XJ, et al. Does increased hepatitis B vaccination dose lead to a better immune response in HIV-infected patients than standard dose vaccination: a meta-analysis? *Int J STD AIDS* 2013;24:117–22.
52. Launay O, van der Vliet D, Rosenberg AR, et al. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. *JAMA* 2011;305:1432–40.
53. Gatanaga H, Hayashida T, Tanuma J, et al. Prophylactic effect of antiretroviral therapy on hepatitis B virus infection. *Clin Infect Dis* 2013;56:1812–9.
54. Sheng WH, Chuang YC, Sun HY, et al. Prophylactic effect of lamivudine-based antiretroviral therapy on incident hepatitis B virus infection among HIV-infected patients. *Clin Infect Dis* 2013;57:1504–6.
55. Fierer DS, Uriel AJ, Carriero DC, et al. Liver fibrosis during an outbreak of acute hepatitis C infection in HIV-infected men: a prospective cohort study. *J Infect Dis* 2008;198:683–6.
56. Luetkemeyer A, Hare CB, Stansell J, et al. Clinical presentation and course of acute hepatitis C infection in HIV-infected patients. *J Acquir Immune Defic Syndr* 2006;41:31–6.
57. van de Laar TJ, van der Bij AK, Prins M, et al. Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. *J Infect Dis* 2007;196:230–8.
58. Gambotti L, Batisse D, Colin-de-Verdiere N, et al. Acute hepatitis C infection in HIV positive men who have sex with men in Paris, France, 2001–2004. *Euro Surveill* 2005;10:115–7.
59. Matthews GV, Hellard M, Kaldor J, et al. Further evidence of HCV sexual transmission among HIV-positive men who have sex with men: response to Danta, et al. *AIDS* 2007;21:2112–3.
60. van de Laar TJ, Matthews GV, Prins M, et al. Acute hepatitis C in HIV-infected men who have sex with men: an emerging sexually transmitted infection. *AIDS* 2010;24:1799–812.
61. Hsu CS, Hsu SJ, Lin HH, Tseng TC, Wang CC, Chen DS, et al. A pilot study of add-on oral hypoglycemic agents in treatment-naïve genotype-1 chronic hepatitis C patients receiving peginterferon alfa-2b plus ribavirin. *J Formos Med Assoc* 2014;113:716–21.
62. Hayes CN, Chayama K. Emerging treatments for chronic hepatitis C. *J Formos Med Assoc* 2015;114:204–15.
63. Ndimbie OK, Kingsley LA, Nedjar S, et al. Hepatitis C virus infection in a male homosexual cohort: risk factor analysis. *Genitourin Med* 1996;72:213–6.
64. Melbye M, Biggar RJ, Wantzin P, et al. Sexual transmission of hepatitis C virus: cohort study (1981–9) among European homosexual men. *BMJ* 1990;301:210–2.
65. Buchbinder SP, Katz MH, Hessel NA, et al. Hepatitis C virus infection in sexually active homosexual men. *J Infect* 1994;29:263–9.
66. Sun HY, Chang SY, Yang ZY, et al. Recent hepatitis C virus infections in HIV-infected patients in Taiwan: incidence and risk factors. *J Clin Microbiol* 2012;50:781–7.
67. Lin AW, Wong KH, Chan K. More safer sex intervention needed for HIV-positive MSM with higher education level for prevention of sexually transmitted Hepatitis C. In: *HIV Drug Therapy Glasgow 2014 in Glasgow, UK*; 2014. p. 131 [Abstract].
68. Nishijima T, Shimbo T, Komatsu H, et al. Incidence and risk factors for incident Hepatitis C infection among men who have sex with men with HIV-1 infection in a large Urban HIV clinic in Tokyo. *J Acquir Immune Defic Syndr* 2014;65:213–7.
69. Dougan S, Evans BG, Elford J. Sexually transmitted infections in Western Europe among HIV-positive men who have sex with men. *Sex Transm Dis* 2007;34:783–90.
70. Streatfield PK, Khan WA, Bhuiya A, et al. HIV/AIDS-related mortality in Africa and Asia: evidence from INDEPTH health and demographic surveillance system sites. *Glob Health Action* 2014;7:1–11.

71. Chang YH, Liu WC, Chang SY, et al. Associated factors with syphilis among human immunodeficiency virus-infected men who have sex with men in Taiwan in the era of combination antiretroviral therapy. *J Microbiol Immunol Infect* 2014;**47**: 533–41.
72. Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. *AIDS* 2007;**21**:983–91.
73. Vogel M, van de Laar T, Henke J, et al. Cluster of acute HCV genotype 4 infections among HIV-positive men who have sex with men in Germany. In: *60th Annual Meeting of the American Association for the Study of the Liver in Boston, USA*; 2009. p. 785 [Abstract].
74. Fierer DS, Fishman S, Uriel AJ, et al. Characterization of an outbreak of acute HCV in HIV-infected men in New York City. In: *16th Conference on Retroviruses and Opportunistic Infections in Montreal, Canada*; 2009. p. 802 [Abstract].
75. Chan DP, Lin AW, Wong KH, et al. Inferring the transmission dynamics of acute hepatitis C virus infection in HIV-positive MSM in Hong Kong. In: *8th IAS Conference on HIV Pathogenesis, Treatment and Prevention in Vancouver, Canada*; 2015 [Abstract].
76. Zhang X, Wang C, Hengwei W, et al. Risk factors of HIV infection and prevalence of co-infections among men who have sex with men in Beijing, China. *AIDS* 2007;**21**:553–7.
77. An MH, Han XX, Liu J, et al. Study on the rates of infection and spontaneous clearance on HCV among HIV-infected men who have sex with men in China. *Zhonghua Liu Xing Bing Xue Za Zhi* 2013;**34**:15–8.
78. Zhao YS, Su SJ, Lv CX, et al. Seroprevalence of hepatitis C, hepatitis B virus and syphilis in HIV-1 infected patients in Shandong, China. *Int J STD AIDS* 2012;**23**:639–43.
79. Lim RB, Tan MT, Young B, et al. Risk factors and time-trends of cytomegalovirus (CMV), syphilis, toxoplasmosis and viral hepatitis infection and seroprevalence in human immunodeficiency virus (HIV) infected patients. *Ann Acad Med Singapore* 2013;**42**:667–773.
80. Hughes SA, Wedemeyer H, Harrison PM. Hepatitis delta virus. *Lancet* 2011;**32**:211–9.
81. Stroffolini T, Ferrigno L, Cialdea L, et al. Incidence and risk factors of acute Delta hepatitis in Italy: results from a national surveillance system. SEIEVA Collaborating Group. *J Hepatol* 1994;**21**:1123–6.
82. Liaw YF, Chiu KW, Chu CM, et al. Heterosexual transmission of hepatitis delta virus in the general population of an area endemic for hepatitis B virus infection: a prospective study. *J Infect Dis* 1990;**162**:1170–2.
83. Chang SY, Yang CL, Ko WS, et al. Molecular epidemiology of hepatitis D virus infection among injecting drug users with and without human immunodeficiency virus infection in Taiwan. *J Clin Microbiol* 2011;**49**:1083–9.
84. Soriano V, Grint D, d'Arminio Monforte A, et al. Hepatitis delta in HIV-infected individuals in Europe. *AIDS* 2011;**25**:1987–9.
85. Hung CC, Wu SM, Lin PH, et al. Increasing incidence of recent hepatitis D virus infection in HIV-infected patients in an area hyperendemic for hepatitis B virus infection. *Clin Infect Dis* 2014;**58**:1625–33.
86. Lee CY, Tsai HC, Lee SS, et al. Higher rate of hepatitis events in patients with human immunodeficiency virus, hepatitis B, and hepatitis D genotype II infection: a cohort study in a medical center in southern Taiwan. *J Microbiol Immunol Infect* 2015;**48**:202–7.
87. Liu W, Lu C, Yang Z, Chang S, Hung C, Chen P, et al. Seroepidemiology of hepatitis E virus infection among men who have sex with men in Taiwan. In: *Interscience Conference in Antimicrobial Agents and Chemotherapy*; Sep 9–Sep 12, 2012. San Francisco. Slide Session V-1238.
88. Sridhar S, Lau SK, Woo PC. Hepatitis E: a pathogen of re-emerging importance. *J Formos Med Assoc* 2015;**114**:681–90.
89. Woo PC, Lau SK, Teng JL, et al. New hepatitis E virus genotype in camels, the Middle East. *Emerg Infect Dis* 2014;**20**:1044–8.
90. Payne BA, Medhi M, Ijaz S, et al. Hepatitis E virus seroprevalence among men who have sex with men, United Kingdom. *Emerg Infect Dis* 2013;**19**:333–5.
91. Cheng SH, Mai L, Zhu FQ, et al. Influence of chronic HBV infection on superimposed acute hepatitis E. *World J Gastroenterol* 2013;**19**:59D4–9.
92. Neukam K, Barreiro P, Macias J, et al. Chronic hepatitis E in HIV patients: rapid progression to cirrhosis and response to oral ribavirin. *Clin Infect Dis* 2013;**57**:465–8.
93. Zhang J, Zhang XF, Huang SJ, Wu T, Hu YM, Wang ZZ, et al. Long-term efficacy of a hepatitis E vaccine. *N Engl J Med* 2015;**372**:914–22.
94. Zhu FC, Zhang J, Zhang XF, Zhou C, Wang ZZ, Huang SJ, et al. Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomized, double-blinded placebo-controlled, phase 3 trial. *Lancet* 2010;**376**:895–902.