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Editorial

Hepatitis B in men who have sex with men and HIV-infected individuals: missed opportunities and future challenges

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Hepatitis B transmission in priority populations continues to occur in Australia despite the availability of a safe, effective vaccine for over 30 years.[1,2] In this edition of *Sexual Health*, Body *et al*.[3] report an incidence of 1.8 hepatitis B virus (HBV) infections per 1000 person years in the Victorian HIV database (VHIVSD), a cohort of HIV-infected individuals receiving care at a tertiary referral hospital in Melbourne. A similar incidence of infection (1.98 per 1000 person-years) was found by Gamagedara *et al*. among men who have sex with men (MSM) attending a community sexual health centre, also in Melbourne.[4]

This incidence of infection is more than 10 times the estimated incidence in the general population[5,6] and is evidence of ongoing transmission in these priority populations despite being part of clinical cohorts and therefore occurring in people linked to care. Both of these recent studies highlighted missed opportunities for screening, vaccination and follow-up testing to ensure the protection of individuals at particular risk of HBV infection.[3,4] This new evidence reinforces the need for a greater focus on comprehensive testing and vaccination of priority populations, including HIV-infected individuals and MSM – particularly given recent reports of increasing sexual risk practices in MSM and corresponding increases in sexually transmissible infections, including HIV.[7]

With an estimated 218,00 people (1.0% of the population) living with chronic hepatitis B (CHB) in 2011,[8] Australia is generally a low-prevalence country, with the main burden of disease experienced by those born overseas in endemic areas, and by Aboriginal and Torres Strait Islander people. MSM are estimated to account for ~4.4% (around 9700 individuals) of those living with CHB[8] and are identified as a priority population for prevention of infection in the First National Hepatitis B Strategy 2010–2013.[9]

The higher incidence of acute HBV infection and prevalence of CHB in HIV-infected individuals and MSM is multifactorial. The increased incidence of infection relates to shared modes of transmission, including sexual, injecting drug use or both. Globally, areas with a high or increasing population prevalence of HIV are often also endemic for CHB, making coinfection with HBV more common in HIV-infected individuals born in these countries who now reside in Australia.[10]

HIV infection is associated with both an increased risk of developing CHB if exposed to HBV and an increased risk of complications, including cirrhosis and liver cancer.[11] In the retrospective cohort reported by Body and colleagues, 23% of patients with incident HBVinfection went onto to develop CHB[3] – far greater than the expected 5% progression observed in immunocompetent adults.[12]

Both studies highlight the need for further improvements in access to HBV testing. In the study reported by Gamagedara *et al.*, ascertainment of immunity status was high but markers of infection were less commonly tested: hepatitis B surface antibody (anti-HBs) was tested in 96% of patients, compared with testing for core antibody (anti-HBc) in 79% and surface antigen (HBsAg) in 26% of patients.[4] As the authors comment, incomplete testing raises the possibility of missed incident and chronic infections. Similarly, Body *et al*. report that HBsAg and anti-HBc testing were not performed in 32% of HIV-positive individuals.[3] The National Hepatitis B Testing Policy released in 2012 recommends testing for all three markers of HBV infection in those at higher risk of CHB, including MSM and HIV-infected individuals.[13] The use of alternative screening algorithms can lead to missing chronic infections, and creates the need for unnecessary vaccination, recall and repeat testing of individual patients. The panel of three tests (HBsAg, anti-HBs and anti-HBc) is Medicare rebatable and is advised for any person at risk of having CHB.

For individuals in the VHIVSD in whom HBV infection was documented, the median estimated time between HIV diagnosis and HBV infection was 4.6 years (range: 4 months to 17 years).[3] These results indicate missed opportunities for prevention through vaccination, and suggest infrequent routine testing to determine anti-HBs status and promote vaccination. Together, they suggest that the prevention of HBV infection in HIV-infected individuals needs greater attention.

Vaccination is recommended for susceptible MSM and HIV-infected individuals.[13,14] However, eligibility for a funded

vaccine for these priority populations varies across Australian jurisdictions (Table 1), with some states promoting the funded vaccine only at a limited number of locations. In several cases, the eligibility criteria and ordering information for funded vaccination is unclear from government websites and resources, representing a barrier to clinician and consumer awareness. Improving the consistency of access to funded vaccination nationally and increasing the uptake of vaccination in these communities are identified priorities in the National Hepatitis B Strategy[9] and ready access to the free HBV vaccine, not surprisingly, increases uptake.[15] Support for and evaluation of novel vaccination strategies, including incentive payments[16] and dedicated clinics,[17] could also be considered to improve vaccination rates in these priority populations.

The course of three vaccinations to confer immunity in immune competent adults presents challenges for standard health care delivery.[18] In HIV-infected individuals, this is further complicated by the reduced efficacy of standard schedules. Double-dose vaccination has been recommended for people with HIV infection for some time,[14] with recent evidence suggesting that four double doses may achieve superior responses.[19] Intradermal administration has also been studied as a way of achieving superior immune responses.[20]

Documenting seroconversion following vaccination is recommended for immunosuppressed individuals including those infected with HIV.[14] Initial anti-HBs titres over 100 mIU mL^{-1} are more likely to result in long-term titres >10 mIU mL^{-1}.[21] The Australian Immunisation Handbook also recommends regular anti-HBs testing for HIV-infected individuals to guide booster immunisation whenever the anti-HBs titre falls below 10 mIU mL^{-1}.[14]

Both of the recent Melbourne-based studies define susceptibility to HBV infection as having an anti-HBs titre of less than 10 mIU mL^{-1} in the absence of evidence of prior infection with HBV.[3,4] Although this is a common definition, this serological pattern can also be observed in those previously successfully vaccinated who still retain memory immunity and who demonstrate an anamnestic response on rechallenge by either the vaccine or by HBV infection.[22,23] This is why no booster vaccination is recommended in immunocompetent individuals who have completed a full course of vaccination (particularly if previously documented to have a protective anti-HBs titre).[24] Thus in both studies, it is likely that the proportion of patients being truly susceptible to HBV infection was overestimated.

Thus the waning of anti-HBs levels in the MSM cohort over a 10-year period reported by Gamagedara *et al*.,[4] which was attributed to decreasing vaccination rates, may also, in part, represent waning antibody titres in a successfully vaccinated cohort. This is particularly so, given that younger MSM would have been eligible for the adolescent catch-up program that commenced in Australia in 1997.[14]

In recent studies of adolescents in Taiwanese high schools, only 48% had anti-HBs titres >10 mIU mL^{-1} 15 years following the introduction of universal infant vaccination. Following boosting with a single dose of vaccine, 94% of students with baseline titres of 1.0–9.9 mIU mL^{-1} demonstrated an anamnestic response, compared with 60% of those with a titre below 1.0 mIU mL^{-1} (60%).[25] Other studies in cohorts in endemic areas in Alaska and China have demonstrated high levels of anamnestic memory more than 20 years after vaccination.[22,23] This could help explain the encouraging finding by Gamagedara and colleagues that anti-HBc positivity was low in MSM aged <30 years and remained so despite waning anti-HBs levels.[4]

The adolescent catch-up vaccination program will cease in Australia in 2014, as the initial birth cohort that received universal infant vaccination reaches 14 years of age. Uptake of the adolescent program has been estimated at ~60%.[26,27] The challenge for clinical services will be to develop clear guidelines on testing and booster immunisation for young MSM and others at higher risk of infection who would have been eligible for universal childhood vaccination, to ensure protection against HBV infection but minimise unnecessary revaccination.

Most current combined antiretroviral therapy (cART) regimens include HBV-active antivirals. In the future, increased treatment of HIV infection at higher CD4 levels in the HIV-infected population may impact on incident HBV and CHB infections in susceptible HIV-infected individuals by both reducing HBV viral load and therefore the incidence of infection, and reducing the chance of progression to chronic infection if exposed. The VHIVSD study had insufficient numbers to analyse the effect of HBV-active cART therapy on incident HBV infection; however, other studies have

Table 1. Recommendations and funding of HBV vaccination of men who have sex with men (MSM) and HIV-infected individuals by state and territory according to health department websites, October 2013

Some websites did not include a specific recommendation in information on the website, however referenced the National Immunisation Handbook

	Website recommendation for MSM	Website recommendation for HIV-infected	Funded for MSM	Funded for HIV-infected individuals	Reference
ACT		√			29
New South Wales	√	√	√	√	30
Northern Territory		√			31
Queensland		√			32
South Australia	√	√	√		33
Tasmania	√				34
Western Australia	√	√	√[A]	√[A]	35
Victoria	√	√		√	36

[A]A free vaccine was available at limited sites such as sexual health clinics only rather than being available through all general practitioners, as cited on the websites referenced.

suggested the possibility of a protective effect.[28] Although the impact of expanded access to HBV-active cART as a form of treatment as prevention of HBV transmission is of interest, this does not replace the need for effective education of individuals about strategies to reduce transmission, and ensuring high levels of immunisation in priority populations against what is currently the only vaccine-preventable blood-borne virus.

Both recent studies from Melbourne have shown a similar incidence of new HBV infections and illustrate challenges to evaluate and then adequately protect individuals at higher risk of HBV infection.[3,4] Prevention of HBV transmission through timely testing and provision of an effective and completed course of vaccination should remain a key component of health care delivery to MSM and HIV-infected individuals, and be adequately funded and supported by clinicians and health departments across Australia.

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