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Need for Increasing Hepatitis A Virus Vaccination Among Patients Infected With Hepatitis B Virus and Hepatitis C Virus

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Severe morbidity can result from viral hepatitis co-infection, particularly in persons with existing chronic liver disease. Vaccination is the most effective way of preventing infection with the hepatitis A virus (HAV) and hepatitis B virus (HBV). Persons with chronic liver disease are currently recommended by the Advisory Committee on Immunization Practices to receive the hepatitis A (HepA) and hepatitis B (HepB) vaccines if they have not previously been vaccinated. Recently, the Advisory Committee on Immunization Practices approved language clarifying that all patients with hepatitis C virus (HCV) infection are recommended for HepB vaccination[1] and that persons with HBV and HCV infections should also be specifically considered for vaccination against HAV.[2,3]

Recent large outbreaks of HAV related to foodborne[4,5] and ongoing person-to-person exposures have resulted in substantial rates of morbidity and mortality.[5–7] Poor HepA vaccine coverage among adults, combined with decreased childhood exposures to HAV since childhood vaccination initiation in 1996, have resulted in a low population immunity as measured by the prevalence of antibody to HAV (anti-HAV).[8] Among adults age ≥18 years with chronic liver conditions participating in the 2014 and 2015 National Health Interview Survey, for example, only19.4% reported having received 1 dose and 11.5% received 2 doses of HepA vaccine. Even among those with ≥10 provider visits, only 13.8% had received two doses of HepA vaccine, indicating missed opportunities for vaccination.[9]

The 1999 through 2012 National Health and Nutrition Examination Survey (NHANES) revealed that the overall anti-HAV prevalence among adults aged ≥20 years was about 25%.[8] In the United States, immunity to HAV is greatest among the cohort of young people born after the 1996 recommendation for pediatric vacci-nation of children residing in areas of high transmission or incidence, particularly the cohort of children subject to the 2006 recommendation for universal pediatric HepA vaccination. Data from NHANES 2007 through 2012 showed 60% anti-HAV positivity among those aged 2 to 11 years in contrast with 16% to 18% among those aged 30 to 49. In earlier NHANES data from 1999 through 2006, only 21.4% of children aged 2 to 11 years had tested anti-HAV positive.[8] Data from the National Immunization Survey—Child for 2016 revealed that 86% of children aged 19 to 35 months had received ≥1 dose of vaccine in 2016.[10] The relatively high vaccine coverage and decreasing acute infection among children has resulted in reduced exposure to HAV for adults and consequently lower immunity among adults. This is exacerbated by poor vaccine coverage among adults, causing decreasing population immunity.

Recent data from the Chronic Hepatitis Cohort Study (CHeCS) at 4 large integrated US health care systems[11] indicates that vaccination rates are far below desired public health

goals. Among 3846 living chronic HBV-diagnosed and 15,471 HCV-diagnosed patients, results were available from total anti-HAV testing performed as part of routine clinical care and vaccination records from the electronic health record at any time in the patient's past medical history through 2015. Updated vaccination records through 2016 were available for patients from 2 sites representing 35% of the cohorts. More than one-half of the HBV cohort patients had testing for anti-HAV and 60% were positive indicating immunity through either vaccination or past infection (Table 1). A similar proportion of HCV-infected patients had anti-HAV testing and 39% were positive. Among patients ever tested for anti-HAV in both HBV and HCV cohorts, significantly higher anti-HAV positivity was found among specific racial and ethnic groups. Higher numbers of patients of Asian/Pacific Islander and Hispanic race/ethnicity (70.3% and56.3%, respectively) were immune to HAV compared with non-Hispanic black or white patients (37.7% and38.4%, respectively; both $P < .001$). These differences could reflect exposure in early life among persons born in countries endemic for both HAV and HBV.

Among patients with HBV in CHeCS never tested for anti-HAV, 17% had evidence of ≥1 dose of HepA vaccine. Among those who tested negative for anti-HAV, 40% had ≥1 dose (Table 1). In total, 44% of the HBV cohort had neither vaccination nor a positive anti-HAV test. Similarly, among HCV patients never tested for anti-HAV, 13% had evidence of 1 dose of HAV or combined HepA/B vaccine. Among those who tested negative for anti-HAV, 38% had ≥1 dose (Table 1). In total, 54% of the HCV cohort had neither vaccination nor a positive anti-HAV test. CHeCS patients' susceptibility to HAV infection has remained largely unchanged; an earlier analysis of cohort data through 2010, at which time 40% of HBV and 44% of HCV patients were HAV susceptible.[12]

Population-based measures available from a variety of sources, including national survey and observational cohort data, show variability in immunity to HAV among US adults. CHeCS chronic hepatitis cohort data demonstrate somewhat better HAV protection among HBV- and HCV-infected persons than NHANES estimates for the general population aged ≥20 years.[8] However, by all measures, HAV protection among US adults is poor, particularly for vulnerable populations with underlying chronic liver disease. These findings, from multiple populations, support current guideline[2] efforts to improve rates of screening for immunity to HAV and subsequent vaccination of vulnerable populations of patients with chronic viral hepatitis.

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Table 1.

HAV Testing and Immunity Status[a]

	HBV cohort (n = 3846), n (%)	HCV cohort (n = 15,471), n (%)
Hepatitis A antibody (anti-HAV) testing		
Never tested	1255 (32.6)	5191 (33.6)
Tested	2591 (67.4)	10,280 (66.4)
Tested, by race/ethnicity		
Asian/Pacific Islander	1484 (68.1)	530 (77.3)
Hispanic	32 (72.7)	372 (72.1)
Non-Hispanic black	358 (71.6)	2095 (66.2)
Non-Hispanic white	503 (65.8)	6695 (66.5)
Other/unknown	214 (59.4)	588 (57.0)
Among those tested		
Anti-HAV negative	1066 (41.1)	6253 (60.8)
Anti-HAV positive	1525 (58.9)	4027 (39.2)
Anti-HAV positive, by race/ethnicity		
Asian/Pacific Islander	1043 (70.3)	281 (53.0)
Hispanic	18 (56.3)	220 (59.1)
Non-Hispanic black	135 (37.7)	825 (39.4)
Non-Hispanic white	191 (38.0)	2447 (36.6)
Other/unknown	138 (64.5)	254 (43.2)
Total never tested for HAV—of these	1255	5191
Received at least one dose of hepatitis A vaccine[b]	212 (16.9)	677 (13.0)
No hepatitis A vaccination	1043 (83.1)	4514 (87.0)
Total tested anti-HAV negative—of these	1066	6253
Received at least one dose of hepatitis A vaccine[b]	422 (39.6)	2379 (38.1)
No hepatitis A vaccination	644 (60.4)	3874 (62.0)
Among total cohort, those with neither	1687 (43.9)	8388 (54.2)

	HBV cohort (n = 3846), n (%)	HCV cohort (n = 15,471), n (%)
vaccination nor positive anti-HAV test		

HAV, hepatitis A virus.

[a]Among 3,846 patients with chronic hepatitis B virus (HBV) infection and 15,471 patients with chronic hepatitis C virus (HCV) infection at 4 large US health systems.

[b]Dates of vaccination ranged from 1995 to 2016.