

## Sliding Down the Cascade of Care for Chronic Hepatitis B Virus Infection

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Globally there are approximately 240 million persons with chronic hepatitis B virus (HBV) infection and an estimated 850,000 in the US.(1, 2) Persons with CHB infection have a high lifetime risk of developing hepatocellular carcinoma, cirrhosis, liver failure and liver related death. Most persons with chronic HBV were infected at birth or during the early years of their lives. In these persons, HBV is usually asymptomatic and only at the time of developing HCC or liver failure, usually in the fifth decade of liver or greater, does this chronic infection become apparent.(3) In the US, 75% of persons with chronic HBV were born in countries where the prevalence of HBV infection ranges from 2% to 15% of the general population. Persons infected as adults are far less likely to develop chronic HBV but more likely to acquire acute icteric hepatitis and recover with lifelong immunity. Subsequently adults with high risk of HBV infection including those with potential occupational exposure and those with life styles or behaviors that put them at risk should be screened and if unexposed, vaccinated. Persons with chronic HBV infection can benefit by not only the available antiviral drugs but also by screening them at the appropriate ages for HCC to detect this tumors when they are small and can be potentially cured.(4) The overall goal is to link persons with HBV to care so that, if they were to develop liver related complications, these could be diagnosed early in order that they might enjoy a long life span.

In this edition of Clinics for Infectious Diseases, an important retrospective multi-center observational study conducted in four large managed care programs, the Chronic Hepatitis Cohort Study (CHeCS) has examined the proportion of persons with chronic HBV infection who are linked to care, the proportion with at least yearly visit for ALT and HBV DNA testing, the proportion with cirrhosis with at least one yearly imaging study and the proportion who were prescribed antiviral therapy for HBV. (5)

What then are the important components of linkage to care for chronic HBV and how does this study address these. Figure 1 is a flow diagram that illustrates what I believe are the important characteristics

in the ideal Cascade of Care for HBV. First of all is the identification of those with HBV infection. The Institute of Medicine has issued two reports, with a third forthcoming, about chronic hepatitis and liver cancer in the US.(6) They have noted that the majority of those with HBV are unaware they are infected and recommend screening persons who have immigrated from endemic areas, most of Asia, Africa, the Pacific Islands, parts of the Caribbean and South America and Eastern Europe be tested for HBV. Also, those offspring of immigrants born in the US but not vaccinated at birth should be tested. The article herein by Spradling et al. does not address how well screening has been incorporated into the CHeCS Study Sites. The CHeCS study does attempt to link to care in their systems all those found to have chronic HBV infection. Each of these large health care systems has liver and infectious disease specialists who are experts at managing chronic HBV. The study then gives of a glimpse at how well management of HBV is going in these settings. In general, success depends on largely two components, provider compliance on ordering the tests and a regular bases, at least yearly according to Practice Guidelines, and patient compliance at showing up for testing and follow-up. Although this study does not separate the number receiving testing into patient and provider compliance specifically, the study did find differences in the proportion of persons who received ALT and HBV DNA testing at least yearly. Those most likely to have these tests performed yearly were insured patients, older individuals, those prescribed antiviral treatment, and males. While testing was statistically most likely to occur in those of White Race/Ethnicity, the actual proportions between these groups was nearly similar.

Finally, it would be important to know what proportion of person who were appropriate for antiviral therapy received it. There are two important components that are needed to answer this questions: what proportion met the current criteria in evidenced-based guidelines for care and what proportion of person who did not meet criteria received antiviral therapy. The natural history of chronic HBV is quite complicated.(7) Unlike hepatitis C infection in which liver disease progresses forwardly in most patients, chronic HBV goes through different phases, from immune tolerant (high viral load, no liver disease) to

immune active (active liver disease) then inactive (low viral load, normal ALT). Furthermore, patients can revert backwards from inactive to immune active, requiring that all patients with HBV be monitored at least yearly at a very minimum. Treatment is recommended by current evidenced based Guidelines for those with elevated ALT and HBV DNA above 2,000 IU/ml who have evidence of at least moderate or severe inflammation or fibrosis.(8)

How can we improve the Cascade of Care for those with chronic HBV infection? First of all, screening can be improved. Currently there are some excellent screening programs that are in place, such as in the San Francisco Bay area, Philadelphia and New York City for example, but most providers are not screening foreign born persons for hepatitis B surface antigen (HBsAg) the serologic marker for active infection. Creative methods using the tools of technology such as prompts in electronic health records (EHR) and messaging apps to remind patients that it's time to be screened are needed. Secondly, more providers need to be trained to perform the initial evaluation persons with newly diagnosed HBV and management for those with stable disease, in the immune tolerant and immune active phases of HBV. A panel of representatives from the major physician and mid-level primary care provider organizations and consultants at a meeting sponsored by the Hepatitis B Foundation developed an easy to use, simple algorithm for primary care providers to screen, vaccinate those seronegative, do the initial evaluation for those detected with chronic HBV and manage those with immune tolerant and inactive phases of HBV.(9) The algorithm gives direction on when to refer patients to specialists if they do not fit the narrow parameters used for the immune active and inactive phases. Primary care providers need to be involved in both screening and follow-up of uncomplicated patients with HBV because there are simply not enough infectious disease and hepatology specialists to manage the large volume of patients with chronic viral hepatitis.

In conclusion, we providers have large task ahead to find, diagnose and link to care those with chronic hepatitis B. Regular monitoring of clinical and laboratory parameters to provide antiviral treatment when indicated, as well as surveillance for those at risk for HCC can decrease the risk of those dying prematurely for liver cancer and liver failure.

**Note:** The author has no reported conflicts of interest.

**Figure Legend:** Fflow diagram of important characteristics in the ideal Cascade of Care for HBV

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Figure 1: Components for the Cascade of Care for Chronic Hepatitis B

