MEETING REPORT

Report on a Single-Topic Conference on “Chronic Viral Hepatitis—Strategies to Improve Effectiveness of Screening and Treatment”

John W. Ward, Anna S.F. Lok, David L. Thomas, Hashem B. El-Serag, and W. Ray Kim

The 2010 Institute of Medicine report on “Hepatitis and Liver Cancer” indicated that lack of knowledge and awareness about chronic hepatitis B (HBV) and C virus (HCV) infections and insufficient understanding about the extent and seriousness of this public health problem impeded current efforts to prevent and control hepatitis B and C. A single-topic conference was held in June 2011 to discuss strategies to improve the effectiveness of screening, care referral, and clinical management of chronic HBV and HCV infections with the ultimate goal of reducing morbidity and mortality from these infections. Various models that have been shown to improve hepatitis screening and effectiveness of hepatitis treatment in the community, including rural settings and populations that have traditionally been excluded due to comorbidities, were presented. Recent advances in laboratory testing, medical management, and new antiviral therapies will not decrease the burden of viral hepatitis if persons at risk for or who are living with viral hepatitis are not aware of the risks, have not been diagnosed, or have no access to care. Systematic changes in our health care delivery system and enhanced coordination of prevention and care services with partnerships between public health leaders and clinicians through education of the public and health care providers and linkage of infected persons with care and treatment services can increase the success of preventing viral hepatitis and the effectiveness of hepatitis treatment in the real world. Implementation of these changes is feasible and will require policy changes, coordination among government agencies, and collaboration between government agencies, health care providers, community organizations, and advocacy groups. (Hepatology 2012;55:307-315)

In January 2010, the Institute of Medicine (IOM) issued a report on hepatitis and liver cancer. The IOM review committee estimated that 3.5 million to 5.3 million persons in the United States are living with chronic hepatitis B virus (HBV) or chronic hepatitis C virus (HCV) infections and an estimated 150,000 persons will die from liver cancer or end-stage liver disease associated with chronic hepatitis B and hepatitis C. The committee found that lack of knowledge and awareness about chronic viral hepatitis on the part of health care and social service providers, and insufficient understanding about the extent and seriousness of this public health problem, impede current efforts to prevent and control hepatitis B and C.

A single-topic conference, cosponsored by the American Association for the Study of Liver Diseases (AASLD) and the Centers for Disease Control and Prevention (CDC), was held on June 4-5, 2011 (http://www.multiwebcast.com/aasld/2011/cdc.aasld.stc.hepatitis/) to discuss strategies to improve the effectiveness of...
screening, care referral, and clinical management of chronic HBV and chronic HCV infections with the ultimate goal of reducing morbidity and mortality from chronic HBV and chronic HCV infection.

Session I: Disease Burden, Epidemiology, Economics, and Opportunities to Prevent and Treat Viral Hepatitis (Harold W. Jaffe, John W. Ward, W. Ray Kim, Marc G. Ghany, John B. Wong)

Based on the National Health and Nutrition Examination Survey (NHANES), an estimated 1%-2% of the US population is chronically infected with HBV or HCV. The annual direct medical care costs of HBV infection have been estimated to be US $205 million to US $1.2 billion and that of HCV infection is estimated at US $1.1 billion. The annual indirect medical care costs related to premature mortality and disability of those age <65 years with chronic HCV infection have been estimated to be US $7.5 billion.

Data from NHANES (1999-2008) estimated that only 0.27% of the US general population aged ≥6 years had chronic HBV infection. However, screening studies conducted among Asian Americans revealed a prevalence of 10%-15%, and a recent study of African refugees living in Atlanta, GA, found a prevalence of 11%. Estimates based on immigration data project the prevalence of HBV in incoming children who were born in 1945-1964. The cohort effect is presumably related to infection through injection drug use (IDU) and health care exposures (e.g., unscreened blood transfusions) in the 1960s to the 1980s. This finding implies that the proportion of patients with HCV who have had the infection long enough to have progressed to cirrhosis and hepatocellular carcinoma (HCC) is increasing. Indeed, age-adjusted mortality from chronic HCV infection and incidence of HCC has continued to increase (Fig. 1). Furthermore, following a period of decline in incidence of HCV infection, there is a resurgence of HCV infection, mainly among young injection drug users.

HBV and HCV screening of at-risk groups is the first step toward care of the infected person and prevention of transmission to others. Yet, a review of records in four medical clinics in the United States found that only approximately 20% of patients had ever been tested for hepatitis B, and only half of those who are expected to be infected with hepatitis C had been diagnosed. Data from randomized controlled trials, cohort studies, and meta-analyses support that antiviral treatment can decrease disease progression particularly among responders. Improved diagnosis, referral, and access to care are needed in order for persons who are chronically infected with HBV or HCV to have an opportunity to benefit from treatment. Economic evaluations suggest that HBV and HCV treatments are cost-effective. HBV treatment needs to be administered for many years, and further research is needed to determine the optimal time to start treatment and the most cost-effective strategy. New HCV treatment with direct-acting antivirals costs more, but this may be offset by a higher rate of response and/or a shorter duration of treatment.

In response to the IOM report, several public policy developments have been initiated. In September 2010, the Trust for America’s Health and AASLD released an issue brief that laid out the challenges presented by viral hepatitis and concrete policy prescriptions for
dealing with those challenges. In May 2011, the US Department of Health and Human Services (HHS) issued “Combating the Silent Epidemic: Action for the Prevention, Care, and Treatment of Viral Hepatitis,” a road map for the nation’s public health response to viral hepatitis (Table 1).

Session II: Education and Community Engagement: Improving the Demand and Acceptance of Viral Hepatitis Prevention and Care Services (Cynthia Jorgensen, Samuel K. So, Charles D. Howell, Bruce E. Landon, Fasiha Kanwal)

A major hurdle in hepatitis prevention and control in the United States is the lack of public and provider awareness, which has led to inadequate public health and health care resource allocation. A recent CDC study showed that both awareness and knowledge of viral hepatitis were extremely low among the public at large, as well as among specific subgroups such as African Americans and Asian Americans. Little was known about the different types, risk factors, and route of transmission of viral hepatitis. Participants were unaware of the asymptomatic nature and hence the need for specific testing for hepatitis virus infection. These data highlight the critical need for educational efforts to improve public knowledge of viral hepatitis.

African Americans and Asian Americans represent two ethnic groups in whom public health and educational efforts are most needed, given the disproportionate burden of viral hepatitis among them. Both groups have higher age-adjusted mortality rates from cirrhosis and HCC than non-Hispanic whites. One potential reason for the bigger impact of viral hepatitis among African Americans is limited access to health care. The problem is compounded by the lower response rates to antiviral therapy for HCV among African Americans, a difference that is in part genetic (i.e., interleukin-28B) and not overcome by the newly approved protease inhibitors. With regard to HBV, the highest burden is among Asian Americans, yet awareness is low. Liver cancer is the second most common cancer among Asian American men, whereas it is the ninth most common among non-Hispanic white men. Reaching Asian Americans for public awareness education on HBV is challenging, because they represent a diverse group with different languages and cultures and include a high proportion of foreign-born individuals with low English proficiency.

As of 2011, eliminating racial disparities in viral hepatitis remains a substantial challenge. Grassroots efforts have been organized by Asian American advocacy groups, which have motivated a small number of local and federal government agencies to engage in
public health campaigns. These programs have focused on education of the public, hepatitis testing of those who have not been screened, vaccination of persons at risk for HBV infection as indicated, and clinical monitoring with preventive and therapeutic interventions in those who are infected. For HCV, proposals have been put forth to refocus screening strategies so that it is guided by demographic characteristics rather than risk behavior.

Although these efforts represent an encouraging recent trend, more fundamental changes at the health care system level is necessary to substantively alter the burden and improve clinical outcomes of viral hepatitis at the national level. These systematic changes may include reengineered care processes, effective use of information technology, implementation of knowledge/skills management, development of health care teams, and coordination of care. This model emphasizes the shared responsibility among public health and primary and specialty care providers in addressing viral hepatitis (Fig. 2). Implementation of such coordination may be facilitated by systematic improvements such as effective application of information technology and use of performance measurement to gauge and improve performance and to track progress at each level of the system.

Physicians and other providers are a key component of the health care system. Motivating them to improve quality of care requires a multifaceted approach which may include self-directed or mandated learning as well as direct and indirect financial incentives. These considerations have increasingly been applied in HCV at the federal government level. The Centers for Medicare and Medicaid Services (CMS) has recognized HCV as a priority area for quality measurement (Table 2). Quality measures are thought to be a prelude to the pay-for-performance (P4P) model in which payment incentives are used to recognize and reward high-quality care and quality improvement. P4P has been shown to produce intended results in some areas of medicine, but the impact of the HCV program remains to be seen. At present, a parallel strategy has not been developed for HBV.

Session III: Screening and Care Referral for Chronic HBV and Chronic HCV: The Entry Point for Counseling and Care (Alain Litwin, Karen E. Kim, Trudy V. Murphy, Daniel Church, Bryce Smith, Jeffrey Levi)

It is estimated that 75% of persons with chronic HCV infection in the United States are unaware that they are infected. In 1998, the CDC recommended anti-HCV testing for high-risk populations; however, barriers to risk assessments including reluctance of providers to ask patients sensitive questions and patient reticence to disclose risk behaviors resulted in very low rate of identification of at-risk persons and subsequent HCV screening.

Screening for HBV is effective in reducing the burden of disease, preventing disease transmission, and providing an opportunity for treatment and HCC surveillance. Many screening programs have been developed and initiated as community-based programs, but they do not provide adequate linkage to care or follow-up for at-risk individuals. In the United States, screening for chronic HBV infection is recommended for all pregnant women, and high rates of screening has been achieved. However, a survey of 190 birthing hospitals in 2005 found that <73% of hospitals had policies for reviewing the pregnant woman’s hepatitis B surface antigen (HBsAg) test result on admission for delivery, or policies to test pregnant women on admission if no documented HBsAg test result is available. Modeling estimates suggest a trend toward an increasing number of infants in the United States born to HBsAg-positive mothers, most of whom came from countries with

Table 2. Medicare Quality Indicators for Hepatitis C

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<tr>
<th>If—</th>
<th>Then—</th>
<th>Evidence (Grade)</th>
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<tbody>
<tr>
<td>Positive anti-HCV</td>
<td>HCV RNA test</td>
<td>II-2</td>
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<tr>
<td>Positive HCV RNA</td>
<td>HCV treatment</td>
<td>I</td>
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<td>If HCV treatment</td>
<td>Genotype test</td>
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<td>If HCV treatment</td>
<td>Viral load pretreatment</td>
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<tr>
<td>If HCV treatment</td>
<td>Viral load at week 12*</td>
<td>I</td>
</tr>
<tr>
<td>Positive HCV test</td>
<td>Hepatitis A vaccination</td>
<td>II-2</td>
</tr>
<tr>
<td>Positive HCV test</td>
<td>Hepatitis B vaccination</td>
<td>III</td>
</tr>
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*Indicators for peginterferon and ribavirin treatment.
intermediate or high prevalence of chronic HBV infection. For 2007, the estimate was >25,000 infants, a significant increase from ≈19,000 in 1993.

In order to overcome the barriers in screening for viral hepatitis, there may need to be systematic integration of screening in clinical and public health settings, as well as policy changes.

Several approaches to increasing referral and screening for HCV have been shown to be effective, such as the use of brief HCV risk screeners, electronic medical records, and a database risk algorithm. In clinical settings with a high prevalence of infection (e.g., methadone clinics), a universal testing strategy can be used. In primary care clinics, both risk-based screener sticker and birth cohort sticker, which prompts physicians to order HCV tests on patients with risk factors and all patients born within a high-prevalence birth cohort (1945-1964), were associated with a high yield of identifying those who test positive (>5%). A good model is the Veterans Administration (VA) HCV program, which integrates HCV screening within routine clinical care. More than 95% of people who come into the VA system for care have been screened for risk factors, and more than 90% of those found to be at risk have been tested for HCV.

There are also several potentially effective approaches to referral: (1) Self-referral, which may help to overcome the barriers of lack of access to primary care providers; (2) HCV case managers and patient navigators who can serve as an important link between patient and medical staff to facilitate appropriate and timely referrals and to connect participants to resources that strengthen commitment to initiate and complete antiviral treatment; (3) telemedicine, such as the project Extension for Community Healthcare outcomes (ECHO), a telemedicine and distance-learning program, demonstrates that specialty care can be extended to remote areas; and (4) Colocated HCV screening, testing, and treatment services. Many successful integrated models of HCV screening and treatment have been described within primary care settings, substance abuse treatment settings, human immunodeficiency virus (HIV) clinics, liver clinics partnering with methadone clinics, and correctional settings.

The 2010 IOM report recommended that the CDC work with state and other local partners to fund comprehensive care for persons at risk for, or infected with, HBV and/or HCV. Correctional services, sexually transmitted disease (STD)/HIV clinics, and mobile health units were identified as appropriate settings for this type of integrated approach. Viral hepatitis screening can be increased through a variety of approaches that harness existing resources within the public health system more effectively. These approaches include policy opportunities for CMS to assure broader screening, reassessment of screening policies by the US Preventive Services Task Force, inclusion of HBV/HCV screening as part of the essential health benefits defined by the Secretary for the health insurance exchanges, and expansion of Health Resources and Services Administration (HRSA) screening efforts at their funded sites such as Community Health Centers and Ryan White HIV clinics. Although each of these strategies will require significant policy changes, they can be implemented within existing budgetary constraints or incorporated under the Affordable Care Act.

The CDC is evaluating an expansion in HCV screening policy from risk-based to a one-time screening of all persons born from 1945-1965. This strategy circumvents the limitations of risk-based approaches by not requiring the discussion of sensitive behaviors.

Session IV: Models of Care for Chronic Viral Hepatitis
(Ronald O. Valdiserri, Brian R. Edlin, Janet M. Durfee, Sanjeev Arora, Shruti H. Mehta, Su H. Wang)

The HHS Action Plan for the Prevention of Viral Hepatitis has four goals (Table 1). To achieve these goals, the plan specifically targets the following: education of providers and communities; expansion of testing, care, and treatment; intensification of surveillance; elimination of vaccine-preventable hepatitis (in particular, mother-to-child transmission of HBV); reduction of hepatitis associated with illicit drug use; and prevention of health care–associated hepatitis.

Achieving the goals of the Action Plan will require improved coordination at all levels of government and the full engagement of health professionals, communities, and private sector partners. The plan commits no additional resources; however, improved priority setting and coordination across federal health programs together with implementation of the Affordable Care Act will address many current unmet needs by offering new opportunities to promote disease prevention and access to quality care for persons with viral hepatitis.

Because the majority of HCV infections in the United States were acquired through IDU, efforts to combat chronic liver disease must comprehensively address that population. Nonetheless, there are numerous challenges. Patients suffer a disproportionate
burden of poverty, homelessness, mental illness, stigmatization, and competing priorities. Physicians who have experience treating HCV infection may not be sufficiently experienced in delivering care to IDUs and vice versa. At the level of health care services, challenges include fragmentation of substance abuse treatment and other medical care, lack of health insurance, transportation, and even identification of infection through testing and counseling.

To overcome these challenges, innovative health care delivery models have been tested such as the Multidisciplinary Integrated Care Program for Substance Using Persons in New York. For persons actively using illicit drugs, the program brings together persons with experience in substance abuse and HCV treatment and addresses common concurrent conditions like mental illness.

The VA also has tested models for delivering care for the estimated 165,000 veterans in care with HCV infection. Approximately 14% of HCV-infected veterans are known to have cirrhosis, and there has been a steady increase in the number with HCC and/or liver-related deaths; however, only 23% of veterans with HCV report having ever been treated, and reasons for not providing treatment include psychiatric disease, substance abuse, advanced liver disease, comorbid disease, and patient issues. Patients who had integrated psychiatric and medical care were more likely to complete evaluation for and to start HCV treatment than other patients with mental health issues. The VA remains a model for what could be possible with a national health plan.

An innovative statewide program for delivery of HCV care in New Mexico used a disease management model via teledmedicine. Health care workers in 21 rural clinics were trained, and the SVR rates to HCV treatment in these clinics were comparable to that achieved by patients treated at the University of New Mexico clinic.

To respond to the large number of foreign-born persons with chronic hepatitis B in New York, NY, innovative programs have been implemented at the Charles B. Wang Community Health Center. More than 8900 persons were screened for HBV infection between 2004 and 2009, and 11.7% were found to be positive for HBsAg for the first time. Using a chronic care model that includes an integrated electronic medical record, a cohort of ≈4500 persons with chronic HBV infection is followed. A special program targets pregnant women to prevent mother-to-infant transmission of HBV. Coordination of care is greatly enhanced by an electronic medical record that provides reminders for key elements of monitoring and treatment.

It is also instructive to consider how models of care used for HIV and other chronic medical conditions might inform the response to viral hepatitis. Much of the HIV care in the United States is delivered in dedicated treatment centers. Funded by HRSA through the Ryan White Care Act, these clinics are able to deliver comprehensive services that include primary care as well as substance abuse care, mental health care, social services, palliative care, and pharmaceutical assistance. Teams of health care workers deliver the care in patient-centered “medical homes” where HIV-related mortality and morbidity has been substantially reduced. Other strategies have also been tried, such as traditional consultative models, remote consultative services (hotlines via telephone), joint nurse practitioner–physician teams, and integrating general medicine or HIV treatment expertise into an existing chronic care setting.

Another model of care that has been applied to other chronic conditions, and more recently to HIV, is the Chronic Care Model, which recognizes that health efforts must be distributed across the community, patients, and health system (Fig. 3). A key emphasis is on motivating patients to have a significant role in their own health care and keeping providers informed with respect to guidelines.

Session V: Standards of Viral Hepatitis Care and Treatment—From Efficacy to Effectiveness
(Mark Sulkowski, Anna S. Lok, Hashem B. El-Serag, John W. Ward)

Advances in the treatment of chronic hepatitis B and hepatitis C, along with surveillance for HCC can improve patient outcomes. However, the efficacy (i.e., interventions observed under carefully controlled conditions) of therapeutic interventions and screening demonstrated in clinical trials do not always reflect the effectiveness (i.e., utility of an intervention in routine clinical settings) of those interventions in routine practice.

Seven therapies have been approved for treating chronic hepatitis B. These treatments suppress HBV replication and result in hepatitis B “e” antigen seroconversion, alanine aminotransferase normalization, and histologic improvement in some patients.

In May 2011, the first generation of HCV nonstructural 3/4A protease inhibitors, Telaprevir and Boceprevir, were licensed for clinical use in the United States. Compared with peginterferon/ribavirin therapy alone, the addition of Boceprevir or Telaprevir increased sustained
viral response rates from 38% to 63% and 46% to 79%, respectively. Guided by patients’ on-treatment HCV RNA level, treatment duration can be as short as 24-28 weeks for patients with rapid viral response.

Despite the proven efficacy of hepatitis B and hepatitis C therapies, several factors limit the impact of these advances on improving outcomes for persons in routine clinical care, including the low percentage of persons aware they are infected (approximately 35% for HBV and as few as 25% for HCV); low rates of referral to care and treatment (40% and 21% for HBV and HCV infection, respectively); inadequate number of clinicians trained to treat infected patients; and high cost of therapy. As a result, of the 3.5 million to 5.3 million persons chronically infected with viral hepatitis in the United States, fewer than one in five are receiving therapy that can potentially prevent adverse clinical outcomes.

Additional challenges hamper efforts to treat patients with viral hepatitis. For instance, certain HCV-infected patients are not candidates for the newly available regimen and the potential for drug–drug interactions and significant adverse events may compromise treatment outcomes. In addition, drug resistance can diminish the efficacy of treatment for both hepatitis B and hepatitis C. The lengthy duration of time required to treat viral hepatitis, particularly hepatitis B, increases the likelihood of missed doses, which can lead to viral mutations and diminished response to available medications.

HCC is the fastest rising cause of cancer-related death in the United States, where most HCC is caused by chronic infection with HCV (47%), HBV (15%), or both types of viral hepatitis (5%). Several studies have demonstrated the efficacy of periodic HCC screening to detect tumors at an earlier stage, increase the likelihood that patients will receive potentially curative therapy, and reduce cancer-specific mortality compared with patients detected with symptomatic HCC. However, implementation of HCC screening in clinical practice is poor. In a recent study of 13,002 HCV-infected veterans diagnosed with cirrhosis during 1998-2005, <50% were screened for HCC within the first year of diagnosis, and only 12% received annual HCC screening during the 3 years following diagnosis.

Action can be taken at the societal and provider level to improve the effectiveness of viral hepatitis treatment and HCC screening in clinical settings. At the societal level, changes in health care policies and reimbursement can increase access to viral hepatitis screening, care, and treatment, and community education can motivate persons to seek recommended prevention and care services. At the provider level, better educating health professionals about recommendations for viral hepatitis testing and HCC screening, and increasing their awareness of available therapeutic options will improve testing and treatment rates, as will use of clinical decision aids. Logistical barriers (e.g., adherence to a protocol of multiple tests and treatment over a prolonged period and access to expensive therapy) also must be addressed to improve the effectiveness of viral hepatitis-related testing and treatment. Finally, research is needed to increase therapeutic options and identify those models of care that will close the gap between results demonstrated in clinical trials and those achieved in clinics across the country. Table 3 summarizes key actions for physicians and other health care providers toward improved control of viral hepatitis.

**Conclusion**

The burden of disease from viral hepatitis is large and is projected to increase over the next several decades. Cost-effective interventions (e.g., vaccination, screening, and linking infected persons to quality care...
and treatment) can stop transmission, reduce disease progression, and decrease the burden of liver disease; however, many persons at risk for or are living with viral hepatitis do not benefit from these lifesaving interventions because they are unaware of the risks, have not been diagnosed, or have no access to care, resulting in substantial health disparities. This status quo is unacceptable and can be improved, particularly in light of recent advances in laboratory testing, medical management and the approval of new antiviral therapies. These interventions, coupled with innovative public health education and testing strategies, can dramatically improve health outcomes. However, the success of such an effort within the clinic and public health setting will require enhanced coordination of prevention and care services involving diverse components of the health system. The AASLD–CDC Single-Topic Conference on Viral Hepatitis served to promote this type of coordination.

References