JOHNS HOPKINS MEDICINE
eLITERATURE REVIEW™
eViralHepatitis Review
Jointly presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing
Supported by educational grants from Bristol-Myers Squibb, Gilead Sciences, Inc., and Merck & Co, Inc.

VOLUME 4 - ISSUE 10

LISTEN TO PODCAST | DOWNLOAD PODCAST | PHYSICIAN POST-TEST | NURSE POST-TEST

New Approaches to the Diagnosis and Management of Chronic HBV Infection

Our guest authors are Kenneth Sherman, MD, PhD , Professor of Medicine and Nadeem Anwar, MD, Associate Professor of Medicine at the University of Cincinnati College of Medicine.

After participating in this activity, the participant will demonstrate the ability to:

- Discuss the use of new assays (HBsAg) to identify various stages of HBV infections.
- Discus the role of newer assays and predictive algorithms in assessing the outcomes and management in HBV infection.
- Discuss risk factors associated with reactivation of HBV infection.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of New Approaches to the Diagnosis and Management of Chronic HBV Infection in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 4, Issue 9 eViralHepatitis Review newsletter—Chronic Hepatitis B Infection: New Approaches to Diagnosis and Management.

Unlabeled/Unapproved Uses

Dr. Sherman and Dr. Anwar have indicated that there will be no references to the unlabeled or unapproved uses of drugs or products, with the exception of tenofovir alafenamide, or TAF, which at the time of this recording has not been approved for the treatment of hepatitis B in the United States.

MEET THE AUTHORS

Kenneth Sherman, MD, PhD
Professor of Medicine
University of Cincinnati College of Medicine
Cincinnati, Ohio

Nadeem Anwar, MD
Associate Professor of Medicine
University of Cincinnati College of Medicine
Cincinnati, Ohio

Guest Faculty Disclosure

Dr. Sherman has indicated that he has served as a consultant/advisor to MedImmune and received grant and/or research support from MedImmune and Innovio.

Dr. Anwar has indicated that he has no financial interests or relationships with any commercial entity whose products or services are relevant to the content of this presentation.

Release Date:
July 14, 2016

Expiration Date:
July 13, 2018

LISTEN TO PODCAST NOW | DOWNLOAD PODCAST | SUBSCRIBE NOW | PHYSICIAN POST-TEST | NURSE POST-TEST

OTHER RESOURCES

Download the podcast transcript

Go to the companion newsletter

PROGRAM DIRECTORS

Mark S. Sulkowski, MD
Professor of Medicine
Medical Director, Viral Hepatitis Center
Divisions of Infectious Diseases and Gastroenterology/Hepatology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Raymond T. Chung, MD
Director of Hepatology and Liver Center
Vice Chief, Gastroenterology Kevin and Polly Maroni Research Scholar
Massachusetts General Hospital Harvard Medical School
Boston, Massachusetts

Julie McArthur, MS, CRNP
Adult Nurse Practitioner
Division of Infectious Disease
Johns Hopkins University School of Medicine
Baltimore, Maryland

Podcast Transcript

BOB BUSKER: Welcome to this *e*ViralHepatitis Review podcast.

I'm Bob Busker, managing editor of *e*ViralHepatitis Review. We're here with Dr. Kenneth Sherman, professor of medicine, and Dr. Nadeem Anwar, associate professor of medicine, and both our guests are from the University of Cincinnati College of Medicine. Our discussion today is on the clinical implications of their recent newsletter issue on New Approaches to the Diagnosis and Management of Chronic Hepatitis B Infection.

***e*ViralHepatitis Review is jointly presented by the Johns Hopkins University School of Medicine, and the Institute for Johns Hopkins Nursing. This program is supported by educational grants from Bristol-Myers Squibb, Gilead, and Merck.**

Learning objectives for this audio program include:

- **Discuss the use of assays such as the hepatitis B surface antigen to identify the various stages of HBV infection.**
- **Explain the role of newer assays and predictive algorithms in assessing the outcomes and management of HBV infection.**
- **Describe the risk factors associated with reactivation of HBV infection.**

Dr. Sherman has indicated that he has served as a consultant/advisor to MedImmune and received grant and/or research support from MedImmune and Innovio. Dr. Anwar has indicated that he has no financial interests or relationships with any commercial entity whose products or services are relevant to the content of this presentation. Our guests have indicated that there will be no references to the unlabeled or unapproved uses of drugs or products, with the exception of tenofovir alafenamide, or TAF, which at the time of this recording has not been approved for the treatment of hepatitis B in the United States.

Dr. Sherman, Dr. Anwar, thank you both for joining us today.

DR. SHERMAN: I'm delighted to be here.

DR. ANWAR: Thank you for the opportunity.

MR. BUSKER: In your newsletter issue, doctors, you reviewed some of the recent publications describing the role of assays and biomarkers, and in particular the use of the hepatitis B surface antigen, to help identify the various stages of HBV infection. Today I'd like to focus on how the information you presented might impact clinical practice. So if you would, Dr. Anwar, start us out with a patient scenario.

DR. ANWAR: We have a 38 year old gentleman of Cambodian descent who is seen for a consultation with a diagnosis of chronic hepatitis B which was acquired at birth. He has no history of jaundice, malaise, abdominal pain, fatigue, or pruritus. He has never been treated for hepatitis B in the past. His lab data shows him to have a viral load of 90 mIU/mL, AST of 25, ALT of 28, hepatitis B surface antigen of 33,000 IU/mL, and his hepatitis B e-antigen is positive. He wants to know if he needs any treatment at this time and how advanced his liver disease is.

MR. BUSKER: In which phase of hepatitis B would you stage this patient at this time? Dr. Sherman?

DR. SHERMAN: As you know, we define a series of disease phases in hepatitis B. This patient is most likely in the immune-tolerant phase, which is characterized by the presence of high viral load with high levels of hepatitis B DNA in serum. His transaminases remain in the normal range. Those two findings taken together typically define the immune-tolerant phase.

In these patients, hepatitis B surface antigen tends to be very high than in other phases of the disease. Treatment is not generally indicated at this stage of disease, but progression is possible, and progression to more active disease should be monitored as time goes on.

MR. BUSKER: Dr. Anwar — progression, or worsening of this patient's chronic hepatitis — what would be the indications of that?

DR. ANWAR: As patients progress to the immune-reactive phase of the disease, they develop symptoms like malaise, abdominal pain and associated fatigue, and they may notice some yellow discoloration of the eyes known as jaundice. The lab data would reflect a rise in the transaminases and bilirubin levels. In the immune-reactive phase, the patient may be able to achieve hepatitis B e-antigen seroconversion to the e-antibody status. At that point the patient will have a decline in transaminases as well as serum DNA level. The surface antigen titers at that point also decrease significantly.

MR. BUSKER: A patient's hepatitis B surface antigen levels — what factors can alter those?

DR. ANWAR: The level of the surface antigen varies from one phase to another during the progression of the disease. It is highest in the immune-tolerant phase, where this gentleman currently is, and when patients move to immune-reactive phase the titers decrease and further decline when the patient achieves the low-replicative phase.

If the patient develops Hepatitis B E antigen negative HBV reactiveation, the viral load is usually in the lower range than that seen in the wild type. Viremia and hence the surface antigen are also lower, in a range similar to that seen in the low replicative phase, and in the presence of cirrhosis, the levels also tend to run lower than in patients who do not have cirrhosis. Advancing age is another factor that decreases the surface antigen.

MR. BUSKER: Dr. Sherman, the workup for the diagnosis and staging of this particular patient — what should that include?

DR. SHERMAN: The initial evaluation should include a detailed history and a physical examination looking for signs of advanced liver disease such as ascites or hepatic encephalopathy. Laboratory testing should be performed and would include assessment of liver function including transaminases; markers of HBV replication; and presence of other possible coinfections, including HIV, hepatitis C, and hepatitis D. We also have to ascertain whether there is concurrent use of alcohol.

Imaging should be performed to assess for the presence of liver cancer, and we have to look for evidence of the degree of hepatic fibrosis. This can be accomplished by various noninvasive measures including FibroScan or biomarkers like FIB-4

or FibroTest. In selected patients, particularly those with signs suggesting the presence of advanced liver disease, a liver biopsy may play an important role and should be considered.

MR. BUSKER: Dr. Anwar, in his current stage, would you consider treating this patient for chronic HBV?

DR. ANWAR: In the immune-tolerant stage the treatment is generally not recommended. The recommendation is to follow the serial ALT levels every six months to monitor for transition over to the immune reactive phase, in which the transaminases start to go up. However, for patients over age 40, a liver biopsy can be performed, and if that shows significant necroinflammation or fibrosis in the setting of elevated DNA fibers, treatment with oral antigen agents can be considered.

DR. SHERMAN: Of course, if the noninvasive testing suggested the presence of cirrhosis, patients are treated regardless of the degree of necroinflammatory activity. So that patient would become a candidate for treatment with a finding of suggested cirrhosis.

MR. BUSKER: Thank you, doctors, for that case and discussion. And we'll return with Dr. Kenneth Sherman and Dr. Nadeem Anwar from the University of Cincinnati College of Medicine in just a moment.

Ms. Julie McArthur
Hello. I'm Julie McArthur, adult nurse practitioner in the Division of Infectious Diseases at Johns Hopkins University. I'm one of the program directors of *e*ViralHepatitis Review.

*e*ViralHepatitis Review is a combination newsletter and podcast program delivered via email to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to hepatologists, infectious disease specialists, primary care physicians, nurses, nurse practitioners, and other clinicians caring for patients with viral hepatitis.

Bimonthly podcasts are also available as downloadable transcripts, providing case-based scenarios to help bring that new clinical information into practice in the exam room and at the bedside.

Subscription to *e*ViralHepatitis Review is provided without charge or prerequisite.

Continuing education credit for each issue and each podcast is provided by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. For more information on this educational activity, to subscribe to and receive *e*ViralHepatitis Review without charge, and access back issues, please go to our website: www.eviralhepatitisreview.org

BOB BUSKER: Thank you, Julie. I just want to jump in here for a moment to tell our listeners about the new GetSMART app for Apple iOS, Android, or desktop. It's about prescribing Extended Release and Long Acting Opioids — GetSMART stands for Safe Means of Administering the Right Therapy. The GetSMART app is available for CME/CE/MOC credit at no cost. You can download it at dkbmed.com/smart. Once more, that's GetSMART at dkbmed.com/smart.

MR. BUSKER: Welcome back to this *e*ViralHepatitis Review podcast. I'm Bob Busker, managing editor of the program. Our guests are Dr. Kenneth Sherman and Dr. Nadeem Anwar from the University of Cincinnati College of Medicine. And we've been discussing New Approaches to the Diagnosis and Management of Chronic HBV Infection. So let's continue, if you would, Dr. Sherman, with another patient scenario.

DR. SHERMAN: Our next patient is a 34 year old man who was born in central Africa. He has a diagnosis of vertically transmitted hepatitis B causing chronic liver disease, and for this he's on an oral antiviral agent. He is being treated with lamivudine, which is still used many places in the world. He's being followed regularly for this disease. His hepatitis B surface antigen is positive, as is his e-antigen. The viral load is undetectable; he's fully suppressed. His ALT is mildly elevated at 42. He read about the new treatments that include newer nucleotide/nucleoside analogs but was somewhat skeptical about thinking about changing from the medication that he's been on for several years. He wanted to learn more about new treatment options and consider whether he should switch to another medication regimen.

MR. BUSKER: That's an interesting question. But let me start off first by asking about the recommendations for monitoring the disease activity in this patient. Dr. Anwar?

DR. ANWAR: In the untreated patient the DNA levels fluctuate during the disease, so any single reading can't predict the disease course. In most labs, the upper limit of transaminases is often listed as much higher than what is considered a normal level in individuals. The upper limit of normal for females and males should be 19 U/L and 30 U/L, respectively. So a level of 42 U/L is more than the upper limit for this gentleman. The treatment decision should be made according to these levels rather than the levels reported in the lab data.

His e-antigen and the e-antibody status should be assessed to see if patient will develop the seroconversion. The rate of HBe seroconversion varies with the age at which the disease was acquired. It ranges from as little as 2% for children younger than 3 years of age, to 8% if the disease was acquired in puberty, and up to 12% if patients become infected in adulthood.

MR. BUSKER: The hepatitis B surface antigen — can that be helpful in predicting response to treatment?

DR. ANWAR: As outlined in the selected paper for this newsletter, the level of surface antigen can be used to follow the disease course. The hepatitis B surface antigen can also be helpful in combination with the HBV DNA in assessing the response to treatment. In the patient described, a drop in the hepatitis B surface antigen as well as the DNA can be used to see if the treatment is working. The hepatitis B surface antigen was lower in patients who have a complete response to the treatment as opposed to patients who have a partial response to the treatment. The hepatitis B surface antigens are generally higher in patients who have the hepatitis B e-antigen positivity than in the patients who have serocoverted to anti-hepatitis B e-antibody.

MR. BUSKER: Dr. Sherman, would you consider this patient to be at risk for hepatocellular carcinoma? If so, how should the screening be done?

DR. SHERMAN: This patient is certainly at risk for development of hepatocellular carcinoma or primary liver cancer. The screening recommendations and surveillance recommendations indicate that he should have an ultrasound performed every six months to detect a developing hepatocellular carcinoma at a stage where it can be effectively managed. Risk factors for hepatocellular carcinoma include male gender, age greater than 40, being born in Sub-Saharan Africa, being immunocompromised, or having a family history of HCC in a first degree relative.

Other factors include elevated HBV DNA levels — that's not present in this patient but it's something that we think about when trying to determine a person's risk. Heavy alcohol use certainly increases risk. Exposure to aflatoxin is another risk factor. Aflatoxin is a common contaminant of peanut and soybean products in Africa and appears to greatly increase the risk of developing hepatocellular carcinoma.

Finally, viral characteristics including the genotype of the virus are risk factors. Genotype C is highly associated with development of liver cancer. Some patients may have other metabolic processes, including metabolic syndrome, that may also independently increase the risk of cancer in someone who has chronic hepatitis B infection.

MR. BUSKER: Dr. Anwar, let me ask you about acute-on-chronic liver failure, or ACLF. You discussed it in your newsletter issue. My specific question is about the effect of oral treatment on the serum surface antigen levels in the ACLF setting.

DR. ANWAR: As with any other type of chronic liver disease, the patient is also at risk of developing acute-on-chronic liver disease. As the paper that we discussed in this newsletter, by Dr. Lai and his group, the response to oral agents in acute-on-chronic liver failure can result in a decrease in the patient's Model for End-Stage Liver Disease (MELD) score, and surface antigen was known to be higher in patients who responded to the treatment to hepatitis B.[1] A high level of pretreatment hepatitis B surface antigen was also found to be a predictor for lower mortality in patients with acute-on-chronic liver disease in chronic hepatitis B.

MR. BUSKER: I want to return to the patient you presented, Dr. Sherman. He's fully suppressed on his current

regimen, but his ALT is elevated. He's read about the newer medications and options, and he wants to know if he should consider switching to a different medication regimen. How would you advise him?

DR. SHERMAN: This patient has been treated effectively for a period of time with lamivudine, and to date it has worked well for him. However, we know from large clinical trials and long-term follow-ups in longitudinal studies that over time this patient has a relatively high risk of developing antiviral resistance and having viral breakthrough with reactivation of disease. For that reason he would be better treated with one of the newer agents that have been in use for the last decade or so, namely entecavir or tenofovir. A newer agent, TAF, is under evaluation now by the Food and Drug Administration and may represent the best choice going forward because of extremely low levels of secondary side effects and adverse events compared to some of the other agents mentioned.

MR. BUSKER: Thank you, doctors. We've got time for one more patient scenario — so if you would, Dr. Anwar …

DR. ANWAR: The next patient is a 58 year old Caucasian female with a history of acute hepatitis B, status post complete resolution, and a recent diagnosis of B cell lymphoma. Chemotherapy is being contemplated for her, and a hepatology consultation was arranged prior to starting the chemotherapy. Her baseline labs show normal transaminases, hepatitis B surface antigen is negative, hepatitis B surface antibody is positive with a titer of 58 mIU/mL (normal < 10 mIU/mL). The hepatitis B DNA is undetectable. Rituximab-based chemotherapy is being planned for her.

MR. BUSKER: So rituximab-based chemotherapy in a patient with prior resolution of her hepatitis B. What are the chances that this patient's HBV could reactivate as a result of her chemotherapy?

DR. SHERMAN: This has been a hot topic in recent years in the fields of hepatology and oncology. The paper that was reviewed in this issue of *e*ViralHepatitis Review specifically addresses this question. Kusumoto and colleagues[2] noted that the risk of HBV activation or reactivation was 8.3% if patients were not treated with a suppressive hepatitis B regimen. If patients were started on a hepatitis B suppressive regimen, no cases of reactivation were observed. The median time for reactivation in the untreated patients was 97 days after enrollment, and the majority of patients whose disease did reactivate had that recurrence within the first year after starting chemotherapy.

MR. BUSKER: The factors associated with the increased risk for HBV reactivation — what's known about those? Dr. Anwar?

DR. ANWAR: Reactivation is more commonly seen in older patients. Also, patients with diffuse, large B cell lymphoma have a higher risk for reactivation. The titers of the anti-hepatitis B surface antibody are also important. People who have titers > 100 mIU have a lower risk of reactivation than patients who have antibody titers < 100 mIU.

Patients who have detectable but not quantifiable levels of HBV DNA at the time of initiation are at higher risk compared to patients who have no detectable virus at the time of initiation of chemotherapy.

MR. BUSKER: In that study by Kusumoto — what did the authors recommend in terms of monitoring for HBV reactivation?

DR. ANWAR: The authors recommended monthly monitoring of the HBV DNA, with special attention to patients at high risk for reactivation, all those risks we just discussed. Initiating antiviral therapy at the earliest sign of reactivation was effective in preventing relapse of the hepatitis, and the anti-hepatitis B surface antibody levels tend to drop during the chemotherapy as shown by another study by Yilmaz. Antibody titers should be monitored while untreated patients are receiving chemotherapy.[3]

MR. BUSKER: Once reactivation of the hepatitis B has been documented, Dr. Sherman, what's the recommendation for treatment?

DR. SHERMAN: Once reactivation occurs, effective treatment can be achieved with nucleoside or nucleotide analogs. When these oral agents are started, HBV DNA as well as ALT levels, should be monitored during treatment, and the goal is to achieve suppression of virus. Older agents like lamivudine have been used successfully, despite their low genetic barrier to resistance, usually because as the reactivation is discovered, the level of viremia is low so early resistance development

is unlikely.

More and more people are using entecavir and tenofovir, which appear to be somewhat more effective, particularly if treatment is continued longer in both treating the primary reactivation and preventing new reactivation or additional reactivation. However, the duration of therapy remains unclear. Many prescribers in this field will generally treat for between two and six months following a reactivation process if the chemotherapy agent has been discontinued. But there is no clear consensus on this, and some people, in fact, continue the drug indefinitely.

MR. BUSKER: Thank you for today's cases and discussion. Before we wrap things up, I'd like to get your thoughts on the future of hepatitis B management. Dr. Anwar, what changes do you see coming?

DR. ANWAR: New treatment modalities are being investigated as we speak. The focus is now on trying to eradicate the virus. So far, the treatments we have available control the virus but cannot eradicate it. Now the focus is on eradicating the virus. Most likely therapy for hepatitis B in the future will incorporate attacking the virus at different sites, including preventing the replication of the virus, preventing cell injury, and eradicating the cccDNA in the nuclei of the infected hepatocytes. Disease monitoring will include following the hepatitis B surface antigen to determine response to treatment. More vigilant screening for patients undergoing chemotherapy for malignancies, especially B cell lymphoma, could decrease the possibility of hepatitis B reactivation in these patients.

MR. BUSKER: Dr. Sherman, your thoughts.

DR. SHERMAN: There are two possible ideal outcomes for hepatitis B with new generations of therapy. One we would call "functional cure" — the clearance of hepatitis B surface antigen. In those patients, reactivation remains possible, but inflammatory disease should be absent, and presumably the risk of hepatocellular carcinoma will be decreased.

We can now occasionally achieve that with current therapies, but its occurrence is uncommon. I agree with Dr. Anwar that targeting multiple sites may increase our chances of doing this, but studies in this area are in their very early stages, and the likelihood of high degrees of success in the next five years appear low. I'm more hopeful in the 10 year horizon.

The other type of cure is the complete eradication of hepatitis B, which involves not just clearance of hepatitis B surface antigen, but actual clearance of the minichromosome, the cccDNA, from the nucleus of hepatocytes and removal or excision of hepatitis B viral DNA that's incorporated into the host chromosome DNA itself. The chance of that seems very unlikely in the near future; it is quite difficult even with some of the newest agents available, such as the newest experimental ideas like the CRISPR/Cas9 system that permits excision of very highly targeted pieces of DNA. But the targeting, getting into hepatocytes and cutting out what you want to cut out without cutting something that's critical to the function of the cell, still appears not easily manageable at this time.

So I have hope in the future. I hope we see a 2020 or 2030 with the complete eradication and cure of hepatitis B possible, but in the meantime we need to continue to identify and manage patients and treat them with the agents we have.

MR. BUSKER: Thank you both for sharing your perspectives. Let's wrap things up now by reviewing what we've discussed today in light of our learning objectives. So to begin, Dr. Anwar: the use of new assays such as the hepatitis B surface antigen, to identify the various stages of HBV infections.

DR. ANWAR: We discussed how the hepatitis B surface antigen is now being investigated as a tool for the monitoring the disease course in patients with chronic hepatitis B. It can be used to determine what phase of hepatitis B infection the patient is going through, and following up the hepatitis B surface antigen over time can alert to the development of immune active disease as well as hepatitis B e-antigen seroconversion.

The variation of the hepatitis B surface antigen can help identify patients with advanced fibrosis, as well as progression in patients with acute and chronic liver disease while on treatment for hepatitis B.

MR. BUSKER: And our second learning objective: the role of newer assays and predictive algorithms in assessing the outcomes and management of HBV infection.

DR. ANWAR: The HBV surface antigen can be incorporated into the labs done for the monitoring of the response of the treatment. It can be combined with the HBV DNA titers to see which patients are having appropriate viral suppression while on treatment. A failure in the drop of the hepatitis B surface antigen and the DNA titers could be an early indication of resistance development and could help guide treatment modification or a decision to stop treatment.

MR. BUSKER: And finally: the risk factors associated with reactivation of HBV infection.

DR. ANWAR: The risk factors for activation of hepatitis B in patients with resolved hepatitis B infection were identified in patients who were started on rituximab-based chemotherapy for lymphomas. The rate of reactivation was identified, and a monitoring protocol was suggested in the study reviewed in this newsletter. The treatment of reactivation was shown to be effective once the diagnosis of reactivation was made.

MR. BUSKER: Dr. Anwar, Dr. Sherman — thank you both for participating in this *e*ViralHepatitis Review Podcast.

DR. ANWAR: Delighted to be a part of this podcast.

DR. SHERMAN: Thank you, Bob, it was my pleasure to be able to be part of this educational experience.

MR. BUSKER: To receive CME credit for this activity, please take the post-test at www.eviralhepatitisreview.org/test.

This podcast is presented in conjunction with the *e*ViralHepatitis Review newsletter, a peer-reviewed literature review certified for CME/CE credit, emailed monthly to clinicians treating patients with viral hepatitis.

This activity has been developed for primary care physicians, gastroenterologists, infectious disease specialists, OB/GYNs, physician assistants, nurse practitioners and nurses, and other clinicians diagnosing or managing patients with viral hepatitis.

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 credit(s).*™ Physicians should claim only the credit commensurate with the extent of their participation in this activity.

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

For nurses, this 0.5 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each podcast carries a maximum of 0.5 contact hour.

This educational resource is provided without charge, but registration is required. To register to receive *e*ViralHepatitis Review via email, please go to our website: www.eviralahepatitisreview.org.

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only.

Use of the names of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing implies review of educational format, design, and approach. Please review the complete prescribing information for specific drugs, combinations of drugs, or use of medical equipment, including indication, contraindications, warnings, and adverse effects, before administering therapy to patients.

***e*ViralHepatitis Review is supported by educational grants from Bristol-Myers Squibb, Gilead Sciences, Inc., and Merck, & Co., Inc.**

This program is copyright with all rights reserved, by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing.

References

1. Lai J, Lin CS, Yang L, Chen SR, Zhang YQ, Ke WM. Pretreatment HBsAg level and an early decrease in MELD score predict prognosis to lamivudine treatment for HBeAg-negative acute-on-chronic liver failure. *Clin Res Hepatol Gastroenterol*. 2014 Jun;38(3):331-336.
2. Kusumoto S, Tanaka Y, Suzuki R, et al. Monitoring of Hepatitis B Virus (HBV) DNA and Risk of HBV Reactivation in B-Cell Lymphoma: A Prospective Observational Study. *Clin Infect Dis*. 2015 Sep 1;61(5):719-729.
3. Yilmaz B, Erdem D, Teker F, et al. The effect of anticancer therapy on anti-hepatitis B antibody titers in patients with haematological malignancies and solid tumours. *J Int Med Res*. 2016 Apr 5. pii: 0300060516638992.

CME/CE INFORMATION

ACCREDITATION STATEMENT

Physicians

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Nurses

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

CREDIT DESIGNATION STATEMENT

Physicians

Podcast: The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses

Podcast: This 0.5 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each Podcast carries a maximum of 0.5 contact hour, or a total of 3 contact hours for the 6 podcasts in this program.

INTERNET CME/CE POLICY

INTENDED AUDIENCE

DISCLAIMER STATEMENT

CONFIDENTIALITY DISCLAIMER FOR CME ACTIVITY PARTICIPANTS

STATEMENT OF RESPONSIBILITY

HARDWARE & SOFTWARE REQUIREMENTS

STATEMENT OF NEED

COMPLETE CME INFORMATION

All rights reserved - The Johns Hopkins University School of Medicine. Copyright 2016.

This activity was developed in collaboration with DKBmed.