Featured Cases: Screening For HCV and HBV Infection In The Clinic

Our guest author is Arthur Y. Kim, MD, Assistant Professor of Medicine at Harvard Medical School in Boston, Massachusetts.

After participating in this activity, the participant will demonstrate the ability to:
- Explain the rationale underlying baby boomer screening for hepatitis C infection.
- Discuss the importance of risk-factor based screening for hepatitis C and hepatitis B infections.
- Summarize the role of the primary care physician in the care of patients living with chronic HBV and HCV infection.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of screening for HCV and HBV infection in the clinic in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 4, Issue 4 eViralHepatitis Review newsletter—Hepatitis: The Need to Screen Now.

Unlabeled/Unapproved Uses
Dr. Arthur Y. Kim has indicated there will be no references to unlabeled or unapproved uses of drugs of products.

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Faculty Disclosure
Dr. Arthur Y. Kim has indicated that his institution has received grant funding for a clinical trial for Gilead Sciences, Inc.

Release Date
February 18, 2016
Expiration Date
February 17, 2018

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MR. BOB BUSKER: Welcome to this eViralHepatitis Review Podcast.

Today’s program is a follow-up to our newsletter on Screening for Chronic Hepatitis Infection. With us today is that issue’s author, Dr. Arthur Kim, assistant professor of medicine at Harvard Medical School.

eViralHepatitis 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 Sciences Inc., and Merck & Co.

Learning objectives for this audio program include:

- Explain the rationale underlying baby boomer screening for hepatitis C infection.
- Discuss the importance of risk-factor based screening for hepatitis C and hepatitis B infections.
- Summarize the role of the primary care physician in the care of patients living with chronic HBV and HCV infection.

Dr. Kim has disclosed that his institution has received grant funding for a clinical trial for Gilead Sciences, Inc. He has indicated that his presentation today will not reference the unlabeled or unapproved uses of drugs or products.

I’m Bob Busker, managing editor of eViralHepatitis Review. Dr. Kim, thank you for joining us today.

DR. ARTHUR KIM: It’s a pleasure to be here, Bob.

MR. BUSKER: In your newsletter issue, doctor, you reviewed the recent literature describing the importance of identifying and screening at-risk individuals for hepatitis C and hepatitis B infection. I’d like to focus our discussion today on how that information can impact clinical practice. So if you would, Doctor — please start us out with a patient scenario.

DR. KIM: A 55 year old man with mild hypertension previously diet-controlled, returns for a physical after two years. He missed his last yearly physical due to being busy at work, but otherwise feels well. His blood pressure turns out to be within acceptable range after he instituted regular daily exercise since his last visit and he has lost 20 pounds. You notice in your automatic reminders as you review the electronic medical record, that the patient has no history of hepatitis C screening, consider screening via hepatitis C antibody.

MR. BUSKER: I want to look at this from the primary care clinician’s perspective. This is a routine checkup on a relatively healthy patient. Why should I screen this patient for hepatitis C? Why not simply ask him about his risk factors? Or just look for symptoms?

DR. KIM: Now that’s a great question, because the patient isn’t particularly endorsing any risk for hepatitis C. However, we’ve learned over the years that risk-factor based screening is notoriously poor to detect hepatitis C infection. And that’s largely because many of the risk factors may have occurred in the distant past or they may even be forgotten by the patient, or due to stigma related to the risk factor, underreported to the provider. After all, what happened 30 years earlier may not be immediately on everyone’s minds today.

Now over half of those in the age group in which this patient is are not aware of their hepatitis C infection; moreover, if you waited for symptoms, that might be too late. Relying on symptoms will be difficult because the infection is silent until the patient has obvious cirrhosis and complications of liver disease.

The other way that primary care physicians have traditionally looked for hepatitis C is reaction to elevated liver function tests; however, this may also be unreliable, as many with chronic hepatitis C infection may actually have values within the normal range. So in the end, this gentleman is within an age group with a four to five times higher risk of hepatitis C infection and therefore becomes a candidate for screening.

MR. BUSKER: Your points are valid, of course. But what priority should a busy PCP give to screening for hepatitis C?

DR. KIM: I agree that primary care physicians are increasingly asked to do more and more for their patients in front of them. There are many conditions for which they may engage in screening, ranging from counseling patients about the need for colonoscopy to seatbelts, and all of these things take time. For hepatitis C, the reason to prioritize screening begins with the way we test.
Testing is very simple. It begins with an antibody test and it’s relatively cheap. It’s only one time, so unlike the need to do regular screenings every let’s say year for something such as cholesterol screening, for the baby boomer cohort, as we call it — those born between 1945 and ’65 — testing for hepatitis C is only needed one time.

And the other reason to prioritize screening is that in the past couple of years there’s been a revolution in the antiviral treatments that are available for hepatitis C. These treatments have become far more efficacious and as well as far more safe than previous interferon based therapies. And the treatments, given their effectiveness, are life-extending for those living with hepatitis C in the vast majority of cases and almost no primary care intervention would be predicted to save as many lives if properly integrated into routine primary care today.

Right now we are in the midst of an epidemic of hepatitis C-related morbidity and mortality among this age group due to infections that occurred 30 years ago, and thus it is a priority to identify those patients before they have liver related problems.

MR. BUSKER: So universal non-risk factor based screening for hepatitis C in the baby boomer population — what are the downsides there?

DR. KIM: Again, acknowledging that primary care physicians are very busy and adding this to the list of things that need to be done can be one downside. The other downside can be that our testing, while the initial test is straightforward with a single hepatitis C antibody test, there is a two-stage process. If someone is positive for that initial screening test, which only measures exposure, one needs to then test for the virus with a hepatitis C RNA test.

MR. BUSKER: Explain that a little more, if you would please.

DR. KIM: What this means is this two-step process will identify those with a hepatitis C antibody that’s positive, but then their hepatitis C RNA is negative; and those individuals are usually either false positive or distantly cleared infection, and in neither case would that have bearing on their current health status. So one will have tested a patient, determined that they’re positive, but from that point on there is no antiviral treatment needed and it may just raise anxiety levels.

In an ideal world we would skip that first test of the antibody and just test for the active infection itself; however, right now the hepatitis C RNA test is a bit too pricey for widespread initial use. There is some work being done to develop either cheaper molecular-based tests to detect the virus or detect the antigen directly.

Another downside to screening for hepatitis C in this population is that there are some areas of the country where antiviral treatments are not available except for those with advanced liver disease. This is largely due to insurance restrictions rather than decisions made by patients and providers, who generally agree to try to eradicate the virus before there are major liver problems. But if you are practicing in an area where treatment is not available then the hepatitis C may not be immediately treatable under the current environment.

Finally, because we’re testing people, primary care physicians will be required to counsel about these false positive tests frequently and this also increases the time involved in screening.

So those are some downsides to this approach to screening those in the baby boomer population.

MR. BUSKER: Point of clarification, doctor. This two-step process — that’s only for those who show positive on the initial antibody test. Is that correct?

DR. KIM: That’s right, Bob. It’s a two-step process only if the hepatitis C antibody is positive at the initial screen, otherwise one doesn’t need to follow up patients who are negative in general.

MR. BUSKER: What should primary care do after a patient has been screened and found to be hepatitis C antibody positive? Take us through the steps, if you would please.

DR. KIM: The first thing a PCP can do is confirm chronic infection by the use of the hepatitis C RNA test. That important step will determine whether a patient requires follow-up for antiviral treatment.

The next step that primary care physicians can provide for their patients would be counseling messages. I find that that primary care physicians can be very much on the front lines of hepatitis C, and some basic knowledge that’s transferred to the patient can be coming from a trustworthy source like the
primary care physician, can be very useful before they reach the specialist, especially because sometimes patients don’t reach specialists.

**MR. BUSKER:** Would you give us little more detail on those counseling messages, please.

**DR. KIM:** So the first counseling messages are regarding transmission. One thing to do is to avoid some misconceptions such as telling patients not to share kitchen utensils or glasses. The virus is not transmitted by saliva, and therefore that doesn’t need to be avoided. We do tell patients to avoid sharing razors or toothbrushes where there can be micro amounts of blood that are contaminated. But other than that, there is not much worry about household transmission.

There’s also a lot of questions that come up regarding sexual transmission risk, and overall, in the usual scenario between monogamous heterosexual couples, we consider that a very low risk for transmission and we meet couples all the time where one partner is positive for the virus and the other partner is negative, despite regular exposures over many years.

In addition to transmission, the primary care physician can also screen for alcohol use more closely, and if there is alcohol use they can provide further counseling. Alcohol is a well-known accelerant of the hepatitis C disease process within the liver, and there may be lifestyle modifications such as avoidance of alcohol that can be recommended. And also, problem alcohol use in particular would be, would require intervention.

Another lifestyle modification that can be important is counseling regarding excess weight. That is because patients can develop concomitant liver disease with fatty liver, or steatohepatitis. And patients who are already overweight could be counseled to decrease their risk by weight loss and also we can counsel patients to avoid further weight gain.

Another area once the patient has tested positive for hepatitis C is to be sure that they are tested for active infection with other viruses, in particular HIV and hepatitis B which share risk factors with hepatitis C, and therefore should be looked for, as there are interventions that can be applied for those who are positive with coinfection with those viruses.

For those who are negative for hepatitis B in particular, one can then vaccinate them as the linchpin of prevention of hepatitis B in this population, and also we typically immunize for hepatitis A virus, as well. There are documented cases of fulminant liver disease due to hepatitis A superimposed on hepatitis C, and given the excellent safety profile and immunogenicity of the hepatitis A vaccine, this should be applied to patients.

Finally, an important step that primary care physicians can engage in is recognizing occult cirrhosis. The reason for this is that those with advanced fibrosis or cirrhosis are in most need for antiviral treatment to interrupt the disease process of hepatitis C, and they can be referred quickly for treatment, and that alters the course of their liver disease. And especially this is true for those living in the baby boomer generation, as their infections are usually many decades ago and they may be hiding this advanced fibrosis or cirrhosis.

So a primary care can perform, for instance, a more detailed physical exam looking for signs of liver disease. There are subtle clues that could be present such as spider nevi. They can do some basic labs and the most basic lab to look for is a lower platelet count that is otherwise unexplained. That could be one of the first signs within a laboratory panel of advanced fibrosis or cirrhosis.

Increasingly, primary care physicians have learned about the noninvasive markers to measure the degree of liver fibrosis for those infected with hepatitis C and if they’re comfortable they can engage in that as well.

**MR. BUSKER:** Now you mentioned referral to a specialist. I think that’s one of the key questions primary care clinicians have. In a patient who has a positive HCV RNA test, should the primary care clinician refer? Or can primary care provide adequate HCV treatment?

**DR. KIM:** That’s a great question, Bob, and I think the future of hepatitis C treatment may increasingly be applied by persons who are not traditional hepatitis C providers such as hepatologists, gastroenterologists and infectious disease experts. I think the provider does need to be knowledgeable about the novel antiviral treatments, and I think it’s worthwhile having the discussion about antiviral treatment for all those who are infected with hepatitis C, even those...
with earlier stage fibrosis. After all, if we’re screening for this infection, if we don’t intervene on the infection with treatment, it defeats a lot of the purpose for screening.

I think those with obvious advanced liver disease should receive specialty care. There are a variety of things done for patients with advanced fibrosis or cirrhosis, such as endoscopy, looking for esophageal varices before they are bleeding, as well as initiation of screening for hepatocellular carcinoma, which is a major source of morbidity and mortality in patients with hepatitis C-related cirrhosis.

Now, it’s true, treatment has become simple and safe enough that a primary care physician who is knowledgeable about the treatments could apply them. There are a variety of online resources and as well as live courses that can equip primary care physicians with the knowledge to treat.

There is also an online hepatitis C guidance provided by the professional organizations of both liver disease, the AASLD, as well as the Infectious Disease Society of America, that has proven useful for those in this novel area of care. Also, there are knowledge networks, specifically trying to equip those on the front lines in health centers in the community that with the knowledge of how to evaluate and treat hepatitis C infection, and the initial studies indicated that treatment can be provided with very similar efficacy as those provided by specialty clinics.

And so this is a very exciting time as treatments have become easier that a primary care physician could become involved in this treatment revolution.

MR. BUSKER: Thank you for that case and discussion, doctor. And we’ll return, with Dr. Arthur Kim from Harvard Medical School, 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 eViralHepatitis Review.

eViralHepatitis 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.

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MR. BUSKER: Welcome back to this eViralHepatitis Review podcast. I’m Bob Busker, managing editor of the program. We’ve been speaking with Dr. Arthur Kim from Harvard Medical School about screening for chronic hepatitis infection, and how the information in his recent newsletter issue can be applied in clinical practice. So to continue: if you would, doctor, please describe another patient for us.

DR. KIM: A 24 year old woman presents to an emergency room with an abscess in her left arm. She has been using intravenous heroin intermittently for the past three years almost entirely with clean needles and syringes. She tested negative for hepatitis C antibody two years earlier.

MR. BUSKER: She tested negative for the HCV antibody previously — does she need to be screened again?

DR. KIM: I think I’ll begin by discussing common arguments against screening this woman for hepatitis C infection. One is, it’s not her primary complaint, she is not presenting in particular to the emergency room for hepatitis C screening. She has other concerns, and there are other competing priorities for her medical and psychosocial care.

Clearly for this woman, she may wish to engage in drug addiction treatment and services to reduce heroin use and the harms associated with particularly intravenous use of a variety of infectious complications. She may be ineligible for treatment
anyway, even if we detected hepatitis C infection, so, for instance, many insurers require at least six months of being clean from intravenous drug use before they agree to treat such an individual. And these are commonly cited reasons that one would not want to screen this patient.

MR. BUSKER: And the arguments for screening her again for HCV infection?

DR. KIM: In the end I would recommend screening this patient for hepatitis C infection for the following reasons. First, the knowledge of status may change her behaviors. It’s pretty clear she’s been trying to stay clean of hepatitis C infection by her pattern of using clean needles and syringes; however, she may still have slipped up in the past, and she also could have engaged in sharing of other paraphernalia used in drug use. And so she may, indeed, be positive despite expressing that low risk. So clearly she, herself, is concerned about acquiring these viruses and the knowledge of her current status may change her behaviors.

If she turned out to be positive there are many individuals who then begin to be less careful, they say, well, I already have hepatitis C so I won’t worry about it from this point on and be less careful. And that would be important to prevent because they are still at risk for additional blood-borne viruses such as HIV. Recently, there is a well-publicized outbreak in the state of Indiana of HIV amongst those who are injecting drugs and clearly that’s a consequence that we need to avoid.

The patient may also misclassify her transmission risk. She may be viremic and able to transmit the virus, or she may actually be cleared of the infection. And so this would also be important information to convey to the patient and may affect her future behaviors.

Some studies in this population of injection drug users do report lower risk-taking behaviors after diagnosis. There seems to be a potential effect of learning their hepatitis C status as motivation for behavioral change. So clearly a bundle of services and screening regarding blood borne viruses for this individual would be important and definitely in addition to hepatitis C screening one would screen her for HIV and potentially other sexually transmitted diseases, as those can also be present at higher rates in this population.

And so there are many opportunities for this patient if one engages her in comprehensive care and I think patients who engage in drug use do appreciate that. There are opportunities for a variety of other preventive messages surrounding the infection complications of drug use.

MR. BUSKER: As we’ve talked about, doctor, baby boomers without current risk factors only need that one time testing. But what about individuals — like the one you’ve presented — who have current risk factors? How often should they be rescreened for HCV infection?

DR. KIM: For those with ongoing or intermittent risk factors, at the moment yearly screening is recommended. Now this is not always done. In the article we do talk about the recent study that looked at those with HIV and looked at hepatitis C screening rates for those already engaged in care. And it’s not always done, even by well meaning and very excellent providers at the centers that were studied in the article by Freiman, et al. So it’s important to institute programs or electronic health reminders, or other approaches to yearly screen individuals who are at high risk such as those living with HIV, particularly men who have sex with men.

And one may consider screening sooner if there are elevated liver function tests, which are often checked regularly in the care of those living with HIV, as well as occasionally with those with other major risk factors such as injection drug use.

It’s pretty clear that implementation of regular screening of individuals has been difficult to implement in practice. For certain groups such as those injecting drugs, there is fragmented care. Patients are often presenting to a variety of institutions, they’re, for instance, emergency rooms, or potentially drug rehabilitation facilities, and the testing can be very scattered, so it’s hard to do overall integrated yearly screening for that individual. And others, you know, for instance for those who are living with HIV where yearly screening is recommended, it can simply be difficult to remember amidst a variety of other aspects of care that the provider is giving.

It may be possible to institute screening in a better fashion in the future. For instance, we typically screen those individuals for syphilis yearly, so why not also include hepatitis C testing for those living with HIV?
MR. BUSKER: Thank you, doctor. Now we’ve been talking about screening for HCV infection, but what about hepatitis B? And let me start out by asking you to summarize for us the major differences between hepatitis C and hepatitis B infections.

DR. KIM: These infections are usually associated together because they do share risk factors: they are transmitted by needle exposures, via sexual transmission, although rarer for hepatitis C in most circumstances, as well as perinatally from mother to child. One major difference, that hepatitis B infection is not considered curable, it integrates into the DNA of cells within the liver, whereas hepatitis C doesn’t have that DNA integration step as part of its life cycle. So hepatitis C is a curable infection.

The other major difference is that hepatitis B vaccine is available and has been in widespread use for well over a couple of decades, and is a highly effective public health measure which has been amazing in dropping hepatitis B rates in many countries. And so those differences are the major ones between hepatitis B and hepatitis C.

MR. BUSKER: Thank you, Dr. Kim. Now, if you would, please bring us a hepatitis B screening scenario.

DR. KIM: A 35 year old married man presents for a new primary care visit. He was born in China and immigrated here when he was a teenager. He recalls being vaccinated when he arrived with a series of three shots for hepatitis B.

MR. BUSKER: This seems simple enough, doctor. He claims he was vaccinated as a teenager, so why should he be screened again for HBV infection?

DR. KIM: Vaccination may not matter if he already had chronic hepatitis B infection, which may have been acquired either perinatally or in youth. In a variety of countries around the world, as well as in the United States before universal precautions were implemented, injections that were potentially contaminated are a common reason why people acquired hepatitis B. Acute infection is usually asymptomatic when really young, so you can’t rely on any history. You can’t just simply ask him whether he had acute hepatitis in the past, and he originates from a high prevalence country, one with very high rates of hepatitis B. This may have not been tested upon immigration, and so given that one can’t rely on symptoms or even abnormal liver function tests, this gentleman is clearly a candidate for screening for hepatitis B.

MR. BUSKER: The patient presented to his primary care clinician. How should the PCP screen for HBV? Is the hepatitis B surface antigen test enough? Or are there other tests? Is there, for example, a hepatitis B panel?

DR. KIM: The hepatitis B surface antigen test is our frontline screening test because it’s the test for active infection. And so it’s considered the most important test. It’s cheap, reliable, very sensitive, and specific.

Now many providers do see the hepatitis B panels that are often available on their ordering sheets and so the panel can be important for a variety of other reasons. If one already has chronic hepatitis B, one needs to characterize it a little bit better and so there’s a variety of tests such as the E antigen test, as well as the hepatitis B DNA levels that could be tested. However, the panel can also be important for other reasons. One can test for markers of exposure using core antibody or surface antibody, and this may be important particularly if patients are immunosuppressed as hepatitis B, even if it’s not active, is potentially a lifelong infection that can reactivate when the immune system is down. And so for those individuals, sending a fuller panel would be very important.

MR. BUSKER: Counseling points for HBV infection — what should the primary care clinician be aware of?

DR. KIM: The primary care physician should be aware to test those living with hepatitis B for both HIV and hepatitis C, as those infections do modulate the natural history of hepatitis B as well as potentially affect the treatment. One should also minimize other liver insults, as we discussed regarding patients for hepatitis C. One needs to avoid excess weight as well as problem alcohol use.

Screening for hepatocellular carcinoma is also more important for hepatitis B, as it may occur in earlier stage infection, and regular screening needs to be implemented based on duration of infection.

And finally, there are a lot of counseling points regarding transmission that can be conveyed to the patient. In particular, one can vaccinate the sexual
partners. In this case the patient’s partner or wife becomes a candidate for both screening, and if negative, to be vaccinated, as well as avoidance of household transmission.

MR. BUSKER: Thank you for today’s cases and discussion, doctor. Let’s wrap things up by reviewing what we’ve talked about today in light of our learning objectives. So to begin: the rationale underlying screening baby boomers for HCV.

DR. KIM: The main reasons for screening baby boomers for hepatitis C infection include the fact that most infections are silent clinically and are unrecognized; and thus, there is value in screening and identifying the infection. There is at least a four-fold risk of infection in this age group compared to the rest of the adult population. And there are highly effective and safe treatments available. Those together make screening for hepatitis C in this population a very valuable intervention that may save many lives in the future.

MR. BUSKER: And our second learning objective: the importance of risk-factor based screening for HCV as well as for HBV.

DR. KIM: There is an increasing rate in several areas of our country of opioid use and many individuals may have silent hepatitis C when exposing themselves particularly to needles. Screening these individuals would have more benefits in terms of counseling regarding transmission to others, and there are many opportunities for multiple preventive messages to be applied for those at high risk for these infections.

The major group for hepatitis B are those who were born in other countries outside of the United States; and these individuals should be targeted for hepatitis B screening, given how silent the infection presents.

MR. BUSKER: And finally: the role that the primary care provider can play in caring for patients living with chronic hepatitis B or chronic hepatitis C infection.

DR. KIM: For hepatitis B, the PCP can help screen highest risk groups such as immigrants from other countries. Also remember to look for signs of past infection in patients who are about to go on immunosuppressive therapies, as the consequences of hepatitis B reactivation can be quite devastating in those individuals.

For hepatitis C, there are several preventive and counseling messages regarding how to prevent transmission, how to prevent further liver disease progression, as well as prevention of other viruses. I think primary care physicians are busy, but they may be a key component in how to intervene in these infections and interrupt the disease course.

These are exciting times for what could be called a revolution of therapeutics for hepatitis C as well as very effective therapies for hepatitis B, and the primary care physician can play a major role in both screening and referral to treatment of these infections, and this will have a major public health impact.

MR. BUSKER: Dr. Arthur Kim from Harvard Medical School — thank you for participating in this eViralHepatitis Review Podcast.

DR. KIM: It really has been a pleasure.

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