



VOLUME 4 - ISSUE 14

LISTEN TO PODCAST

DOWNLOAD PODCAST

PHYSICIAN POST-TEST

NURSE POST-TEST

Extrahepatic Manifestations of Hepatitis C: Screening and Management

Our guest authors are Jordan Feld, MD, MPH and Joel Emery, HBSc, MD, hepatologists from the University of Toronto.

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

- Summarize important extrahepatic manifestations of hepatitis C infection.
- Describe the significant impact of extrahepatic manifestations on patient morbidity and mortality.
- Identify management priorities in patients with extrahepatic manifestations and the impact of hepatitis C eradication.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of Extrahepatic Manifestations of Hepatitis C in the format of case-study scenarios for the clinical practice. This program is a follow up to the [Volume 4, Issue 13 eViralHepatitis Review newsletter - Extrahepatic Manifestations of Hepatitis C: Screening and Management](#).

Unlabeled/Unapproved Uses

Dr. Feld and Dr. Emery have indicated that there will be no references to unlabeled/unapproved uses of drugs or products.

MEET THE AUTHORS



Jordan J. Feld, MD, MPH

Toronto Centre for Liver Disease
Toronto General Hospital
Sandra Rotman Centre for Global Health
University of Toronto
Toronto, Canada



Joel S. Emery, HBSc, MD

University of Toronto
Adult Gastroenterology
Toronto, Canada

Guest Faculty Disclosure

Dr. Feld has indicated that he has received research grant support from AbbVie, Boehringer Ingelheim Pharmaceuticals, Gilead Sciences, Inc., Janssen, Merck & Co., Inc., and Regulus Pharma. He has served as a consultant or advisor for AbbVie, Bristol Meyers Squibb, Gilead Sciences, Inc., Janssen, and Merck & Co.

Dr. Emery 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:

October 27, 2016

Expiration Date:

October 26, 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](#)

NEWSLETTER ARCHIVE

SHARE WITH A COLLEAGUE

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 eViralHepatitis Review podcast.

I'm Bob Busker, Managing Editor of the program. Our discussion today is a follow-up to our newsletter on **Extrahepatic Manifestations of Hepatitis C**. With us today are that issue's authors, Dr. Jordan Feld and Dr. Joel Emery. Both our guests are hepatologists from the University of Toronto.

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 & Company.

Learning objectives for this audio program include:

- Summarize important extrahepatic manifestations of hepatitis C infection.
- Describe the significant impact of extrahepatic manifestations on patient morbidity and mortality.
- Identify management priorities in patients with extrahepatic manifestations and the impact of hepatitis C eradication.

Dr. Feld has indicated that he has received research grant support from AbbVie, Boehringer Ingelheim Pharmaceuticals, Gilead Sciences, Inc., Janssen, Merck & Co., Inc., and Regulus Pharma. He has served as a consultant or advisor for AbbVie, Bristol Meyers Squibb, Gilead Sciences, Inc., Janssen, and Merck & Co.

Dr. Emery 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.

Both our guests have indicated that there will be no references to unlabeled or unapproved uses of drugs or products in today's discussion.

Dr. Feld, Dr. Emery — thank you both for joining us today.

DR. FELD: Thanks a lot for having us. It's a great pleasure to be here.

DR. EMERY: It's a pleasure. Thank you for the opportunity.

MR. BUSKER: In your newsletter issue, doctors, you reviewed some of the recent studies that highlight the most common extrahepatic manifestations of hepatitis C infection and their effects on patient morbidity and mortality. Today I'd like to focus on how that information can impact clinical practice. So start us off, if you would please, Dr. Emery, with a patient scenario.

DR. EMERY: This is a case we saw in our own clinic. It's a 54 year old female with chronic hepatitis C. She has genotype 1B and she's returning for consideration of treatment. She is treatment-experienced, relapsed after treatment with peginterferon and ribavirin, and has known decompensated cirrhosis, with diuretic-controlled ascites.

Her history is significant for mixed cryoglobulinemic vasculitis. She's had skin ulcers, arthralgias, and renal insufficiency. Today when we see her on exam she is hypertensive, blood pressure is 160/80, and she has multiple purpuric skin lesions and splenomegaly. Her labs today in clinic show a hemoglobin of 9.0, platelet count of 118, AST 29 with an ALT of 22. Her INR is calculated to be 1.1 with total bilirubin of 0.8 and albumin of 4.3. We calculate her MELD score to be 6, with a creatinine of 1.3 and an estimated GFR of 44. Her cryocrit is also measured today and it's 13 percent. A urinalysis shows significant hematuria and proteinuria. Because of all these findings we decide to initiate treatment with simeprevir and sofosbuvir, at standard doses, for 24 weeks.

She does improve clinically, however at SVR12, she has evidence of viral relapse with a cryocrit measured at 11%. In addition, she has a return of her joint, skin, and renal manifestations. We again start antiviral therapy with sofosbuvir and ledipasvir, this time for 24 weeks, and she does achieve SVR. Her cryocrit level at week 24 post treatment is 2%. She has resolution of her joint and skin manifestations. Her renal function has improved; the creatinine is measured at 1.1 and eGFR is 55 with no significant proteinuria.

MR. BUSKER: Dr. Feld? Cryoglobulinemia -- define that for us if you would, please.

DR. FELD: Cryoglobulins are antibodies that precipitate in the cold, hence the name cryoglobulins. When they were first recognized, for a long time it was unknown what the cause was. But interestingly, in essential mixed cryoglobulinemia, 90% of people with this disease have hepatitis C infection. So with the discovery of the virus, most cases of cryoglobulinemia were explained. The clinical challenge with these cryoglobulins is that they precipitate. They form immune complexes with antibody binding to antigen directly from the hepatitis C virus, and they precipitate in small blood vessels. Cryoglobulins typically precipitate in the renal vessels, in skin vessels, and vessels supplying nerves, so you can end up with neurologic complications, renal complications, and skin complications; and rarely other organs can be involved.

MR. BUSKER: Mixed cryoglobulinemia — how does that normally present?

DR. FELD: One of the challenges with mixed cryoglobulinemia is, it's often relatively subclinical, so a significant proportion of patients with hepatitis C will have circulating cryoglobulins. Up to about 30% or so will have them if they're sought out and tested for; however, only a minority of those patients will have symptoms that they would be aware of. The common symptoms patients will complain of are arthralgias, as this woman had. They may also develop renal manifestations that can present either as hematuria or proteinuria and occasionally as progressive renal failure. The most common thing we see is asymptomatic skin rash, where patients will have purpuric lesions, typically on the anterior aspects of their shins. These lesions typically are not very symptomatic. Some patients will notice them, but more often we just see a scar, and sometimes we see vasculitic lesions develop.

You get a small amount of hemosiderosis around the lesions, with iron leaking out and staining the skin, so a lot of patients will have a brown pigmentation to their anterior shins, which is often an indication that they have cryoglobulinemia. Although that may be the only thing you notice on physical exam, it's important to then search out the more significant complications like renal disease, neurologic disease, and other manifestations.

What typically happens over the course of cryoglobulinemia is relaxing and remitting episodes. Patients often notice the symptoms — they may be worse in the cold, particularly the skin and joint symptoms — but often patients won't recognize

that association so they just notice that they come and go. The episodes can vary from very mild, asymptomatic manifestations where you just see this type of scarring I was discussing, to full-blown ulceration of the skin and very debilitating neurologic conditions where people may go from mild sensory deficits to actual neuropathies. Likewise, the renal disease ranges from asymptomatic elevation of creatinine or abnormalities in the urinalysis to full-blown renal failure.

This typically is more common in women and tends to present a little bit later in the middle age, 50 to 60s, and the skin is the most commonly involved system.

The next most common thing we see is neurologic and joint symptoms, and then renal disease. It's important to recognize, at least in some individuals, that cryoglobulinemic vasculitis can be life threatening. Patients can have very aggressive vasculitis with severe skin ulcerations, severe neurological conditions, and very rapidly progressive renal failure, which if untreated can be fatal.

MR. BUSKER: Thank you for that background, Dr. Feld. I want to go back to the patient you described for us, Dr. Emery. Your newsletter issue talked about the connection between hepatitis C and cryoglobulinemia. Please apply that to this patient. How are her symptoms related to hepatitis C?

DR. EMERY: As Dr. Feld has noted, the relationship between mixed cryoglobulinemia and hepatitis C is quite strong. We think — although some of the research is ongoing — HCV stimulates B cells. This leads to proliferation of the B cells and then to impaired dysregulation and autoregulation. These B cells can form the immune complexes that lead to clinical vasculitis.

The symptoms that were expressed in our patient were the skin manifestations that are obviously seen, but perhaps more subtle were some of the changes in her renal function. Certainly proteinuria and hematuria can often be mistaken if people aren't looking for them by doing urinalysis, and as we identified she has quite significant hematuria and proteinuria.

Many people may not recognize hypertension as a factor, but mixed cryoglobulinemia can present only with hypertension without any other evidence of renal insufficiency.

Finally, a lot of people would say because she has cirrhosis, her ascites is likely related to that. But because she also has significant proteinuria, it's important to keep in mind that this may also be related to the underlying renal insufficiency.

DR. FELD: I would add that in this woman with what appears to be otherwise very well compensated cirrhosis — in fact, her albumin is normal at 4.3 — it would be a bit surprising to see ascites from her liver disease. So I think, although it's sometimes hard to separate the two, that Joel is absolutely correct that the cryoglobulinemia and the proteinuria are playing a significant role in the development of ascites in this woman.

MR. BUSKER: Management options for this patient? Dr. Feld?

DR. FELD: When we started treating mixed cryoglobulinemia, it was understood that this is driven by the virus, so we should try to target the virus. However, with our old therapies when we started using interferon based therapy, this was very difficult to do, partially because as we've mentioned, this is a B cell disorder. So it's an autoimmune condition, and interferon, which is an immune stimulant, can make the cryoglobulinemia worse.

So the challenge was really the tolerability of the treatment that might make cryoglobulinemia manifestations worse. Patients with advanced cirrhosis like this woman may not tolerate interferon. Still, it was relatively effective, so in patients who could manage to get through the therapy, we did see a very strong correlation between eradicating the virus and having an improvement in their vasculitic symptoms.

The primary goal was try to target the virus — if you could do it, that was successful — but for patients who either couldn't tolerate the treatment or had very aggressive treatment, we had to add rescue therapy with immunosuppressives. That has ranged over time from fairly nonspecific immunosuppressive agents like steroids and azathioprine, to more recently B cell targeting therapy, specifically rituximab, which is shown to be highly effective, at least at inducing remission. However, rituximab does not lead to a long-term, sustained remission because the virus that is stimulating production of the cryoglobulins remains present.

So the goal has been to try to find a strategy that combines antiviral therapy and if needed, adding immunosuppressive therapy. The development of direct-acting antivirals has put us in a situation of rethinking how we address cryoglobulinemic vasculitis and starting to treat this condition earlier, ideally with antivirals, right up front. We hope that by giving these very well-tolerated agents that are highly effective at suppressing the virus, we'll be able to reduce B cell proliferation, reduce cryoglobulinemia, and ultimately lead to viral cure and also to immunological benefits, which notably may be delayed beyond the initial viral suppression.

DR. EMERY: I agree completely. I think there is probably one situation we should add on: in people with very advanced end organ damage, sometimes even therapies like rituximab will not act fast enough. In these situations, plasmapheresis — removing the underlying immune complexes very rapidly to limit further end organ damage — may be indicated.

MR. BUSKER: So Dr. Emery, for this patient — what do you see as her long-term prognosis?

DR. EMERY: This is the big question. Most of the data we have suggests that if you can achieve a virological cure for these patients, from a mixed cryoglobulinemia point of view, they do quite well — that is, if you achieve a virological cure; most likely these people will achieve an immunological and clinical tier where the cryocrits will eventually disappear and eventually have marked improvement in their clinical symptoms.

But I think this goes back to Dr. Feld's point about treating people early, because if there is significant end organ damage before treatment is applied, they may not fully recover. I think the urgency is, if we wait to treat, their end organ damage may get worse, and particularly in our patient's situation, her renal insufficiency.

One final point I think a lot of our listeners will agree with is, she also has cirrhosis. And even though her hep C is cured, she will need ongoing follow-up because of the risk of HCC.

MR. BUSKER: Thank you for that case and discussion. We'll return with Drs. Jordan Feld and Joel Emery from the University of Toronto 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.

Subscription to eViralHepatitis 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 eViralHepatitis 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 eViralHepatitis Review podcast. I'm Bob Busker, managing editor of the program. We've been talking with Dr. Jordan Feld and Dr. Joel Emery from the University of Toronto about recognizing

and managing the Extrahepatic Manifestations of Hepatitis C, specifically about how some of the new information they presented in their newsletter issue can be applied to clinical practice. So let's continue with another patient scenario, Dr. Feld.

DR. FELD: This patient is a 50 year old woman who is evaluated for vague abdominal pain and complaints of early satiety. She describes that she's been increasingly fatigued over the past year but has been otherwise doing pretty well, managing most of her activities of daily living without a problem. Her laboratory values are notable in that she's anemic with a hemoglobin of 9.8. Her white count is also low at 2.8, with a lymphocyte count of 3, and her platelets are reduced as well at 120,000. So she is pancytopenic with mild lymphocytosis.

Her transaminases are close to normal, her AST is 32, and her ALT is 58 with an alkaline phosphatase of 145. An ultrasound shows a normal-appearing liver; however, her spleen is enlarged. She is tested for hepatitis C and found to be hepatitis C RNA positive. Noninvasive testing with transient elastography shows mild F1, or stage 1, fibrosis. At that point there is concern raised about an underlying malignancy, and she has immunophenotyping of her peripheral blood, which is consistent with a splenic marginal zone lymphoma.

MR. BUSKER: Hepatitis C and lymphoma — Dr. Feld, how are they related?

DR. FELD: For a long time it's been recognized that patients with hepatitis C infection have an increased risk of developing non-Hodgkin lymphoma, particularly B cell lymphomas. It was the recognition that these were very specific B cell lymphomas that were highly associated with hep C, particularly splenic and marginal zone low grade lymphomas.

These are relatively indolent lymphomas, but the real connection between hepatitis C and these types of lymphomas was drawn when it was recognized by treating the hepatitis C could result in a regression of the lymphoma. So treating the virus could also improve the outcome of the cancer.

This has been seen relatively infrequently. It's similar to *H. pylori* and MALT lymphoma, but it has not been described with too many other conditions. The rationale is, hepatitis C leads to antigenic stimulation, and these B cell clones sometimes lead to cryoglobulinemia. But even in the absence of cryoglobulinemia, the proliferation then takes on a malignant transformation.

It's thought to be a two-step process, where the hepatitis C is originally driving stimulation of B cells, and then a second insult happens. There's a variety of theories of what that insult might be, but ultimately that leads to an antigen independent proliferation of these B cells in the form of a lymphoma. These can range from the strongest association, or with these relatively rare indolent lymphomas like splenic and marginal zone, but there is also a clear association with even high grade lymphomas like diffuse large B cell lymphoma, the most common type of B cell lymphoma.

MR. BUSKER: Treating indolent lymphomas with antiviral therapy — Dr. Emery, what does the evidence show about the benefits?

DR. EMERY: There's strong evidence that treatment of HCV-associated lymphoma results in clinical cure, and I think this is the real benefit. Now as we have therapies that are well tolerated, specifically direct acting therapy, we hope these agents will have an even more important role in treating indolent lymphomas.

DR. FELD: Patients who developed these lymphomas have often been elderly and would not have tolerated an interferon-based regimen, but they have been successfully treated with direct acting antivirals with both virologic cure as well as an improvement or in some cases even a complete cure of their lymphoma.

MR. BUSKER: What about high grade lymphomas, as opposed to the indolent lymphomas you've just been discussing. Dr. Emery?

DR. EMERY: You definitely want to consider people with high grade lymphomas for chemotherapy, and they should have medical oncology assessment and treatment, but it's after treatment where antiviral therapy becomes important because we know if we treat people with HCV-associated lymphoma, we can prevent relapse.

DR. FELD: An additional point for our oncologic colleagues is screening. Anyone presenting with a B cell lymphoma should be screened for hepatitis C because if it's an indolent lymphoma, treating the hepatitis C may control the lymphoma. And for a high grade lymphoma, as Joel mentioned, it will prevent relapse, which is a critical part of their therapy after they receive chemotherapy.

MR. BUSKER: Thank you for that case and discussion, doctors. We've got time for one more patient scenario — so if you would, Dr. Emery.

DR. EMERY: Our last case is a 48 year old female. She has a history of hepatitis C, phenotype 1A. She also has poorly controlled diabetes and obesity. She is a smoker and has dyslipidemia and hypertension.

She is maintained on metformin, ramipril, atorvastatin, and aspirin. She reports no specific liver symptoms, but she's noted some blistering lesions on her skin, especially in sun-exposed areas, mainly on her hands and fingers.

When we examine her, she has no stigmata of liver disease. Her laboratory investigations reveal a hemoglobin of 12.8, a platelet count of 220, and a creatinine of 0.9. Her AST is 32, her ALT is 69, and her total bilirubin is 0.5. INR is 0.9. A FibroScan identifies F1 fibrosis. She has a liver biopsy, which confirms steatosis, portal inflammation and hepatocyte ballooning, and apoptosis. It's also F1 fibrosis on this scale. An ultrasound also reveals steatosis but otherwise a normal liver.

MR. BUSKER: Porphyrria cutanea tarda and hepatitis C infection. Dr. Feld, how are they related?

DR. FELD: Porphyrria cutanea tarda, or PCT, is not a common extrahepatic manifestation of hepatitis C, but it's a well-recognized one. In fact, about half of people with this condition will have hepatitis C if they're tested for it. This is thought to be related to the hemoglobin degradation pathway and the handling of porphyrin, not the hepatitis C directly. The inflammation in the liver leads to impairment of porphyrin degradation and metabolism pathway, and the porphyrins accumulate in the skin, which makes people develop the skin rash in light-sensitive areas because of the light sensitive porphyrin deposition.

This can happen with other liver diseases. It is sometimes seen with alcohol-related liver disease or iron overload, but in people with hepatitis C, if we can cure the viral infection, we often see resolution of the PCT. If that treatment isn't completely effective, some patients also have to undergo phlebotomy to reduce their iron stores because iron is associated with liver inflammation, which inhibits the enzymes in the porphyrin pathway.

MR. BUSKER: This patient you presented, Dr. Emery — she's diabetic. How does her HCV infection relate to her diabetes?

DR. EMERY: A lot of literature supports a strong relationship with porphyria, but we're starting to learn that there may be a relationship to diabetes itself. It isn't completely understood, but we do know that rates of diabetes are definitely higher in patients with hepatitis C, even when we compare age- and sex-matched populations. We have a couple of theories for this.

First, it's thought that the virus itself may have a direct effect on glucose handling. It also may be that the inflammatory response of having a chronic viral infection promotes diabetes. We also know that treatment of hepatitis C is associated with better diabetic glycemic control, and patients who are treated have better cardiovascular outcomes, which is probably related to the improvement in the diabetes itself.

The papers we discuss in our newsletter issue highlighted the fact that the benefits of HCV eradication at the population level definitely improve nonhepatic outcomes. This is driven by improvement in diabetic outcomes and also in cardiovascular and renal outcomes.

MR. BUSKER: So all in all, Dr. Feld — what factors would you consider when you're assessing this patient?

DR. FELD: As in all patients, I would certainly consider her degree of liver disease, but I think it's notable in this woman that liver disease is far from her primary concern, nor is it the main issue related to her hepatitis C infection. I think we have to think about other factors in this patient.

From a liver perspective, we have to consider the fact that she probably also has nonalcoholic steatohepatitis, or NASH. Her liver biopsy shows evidence of hepatocyte ballooning and significant steatosis, so she has nonalcoholic steatohepatitis, which is probably associated with faster progression of her hepatitis C infection.

Then, as Joel discussed, we also have to think about moving outside the liver and think about the extrahepatic issues here. For this woman who has a number of comorbidities, diabetes is very important. In the long-term we have to put hepatitis C into the context of her risk for cardiovascular complications from diabetes, as well as hyperlipidemia, her smoking history, and her history of hypertension. If we can eradicate this infection, we may be able to improve her diabetic control and reduce her risk of some of these other nonhepatic complications, and also potentially improve her overall quality of life in terms of things like fatigue, ability to concentrate, and other issues that may be affected by the hepatitis C outside the liver.

MR. BUSKER: It seems from what you're saying, Dr. Feld, you'd consider antiviral treatment for this patient, despite her minimal level of fibrosis. Is that correct?

DR. FELD: Absolutely. This is a good demonstration of why we need to think about more than the liver when we talk about hepatitis C treatment. It's very rare to have a cure to an infectious disease or a disease of any kind that we know causes complications and yet restrict therapy to those with only a more severe form of the disease. The idea that people aren't "sick enough" to receive therapies is hard for people infected with hepatitis C to understand, and I think that's not something we are used to doing as medical providers.

This is an area where we're not treating the hep C for her liver, but we're certainly treating the hep C for the other benefits. When we start thinking about the cost effectiveness of these therapies, if we were to take into account some of the extrahepatic manifestations and their consequences, we would see that hepatitis C treatment is even more cost effective than we already know. Although this woman needs to address other comorbidities in her life, her hepatitis C should be treated — ideally cured — and that will hopefully improve her overall outcome.

MR. BUSKER: What about her diabetes? Do you see any potential benefits of antiviral treatment there?

DR. FELD: There may be the immediate benefit of improved glycemic control. In fact, people with early, diet-controlled diabetes sometimes go back to a nondiabetic state. In addition, this woman has NASH, and eliminating the hepatitis C will also slow the progression of NASH in her liver. So she has a number of potential benefits beyond just eliminating the hepatitis C infection from her liver.

MR. BUSKER: Dr. Emery? Your thoughts?

DR. EMERY: I agree with that. The current evidence suggests that not only is diabetes well controlled, but other end-organ complications such as renal disease are decreased when we treat hepatitis C. In addition, important cardiovascular outcomes like stroke and heart attack are also reduced, and even all-cause mortality from those is reduced when we treat patients with diabetes.

MR. BUSKER: Doctors, I want to thank you both for today's cases and discussion. Let's wrap things up now by reviewing the key points of today's podcast in light of our learning objectives. So to begin, Dr. Feld: the important extrahepatic manifestations of hepatitis C infection.

DR. FELD: We reviewed cases involving three important extrahepatic manifestations of hepatitis C infection, mixed cryoglobulinemic vasculitis, non-Hodgkin lymphoma, and diabetes, all of which can be severe complications of this disease.

MR. BUSKER: Our second learning objective: the significant impact of extrahepatic manifestations on patient morbidity and mortality.

DR. FELD: We highlighted with the cases we presented that some of these extrahepatic manifestations can cause serious morbidity and in some cases even mortality, as we saw in severe cryoglobulinemia, lymphoma, and a woman with diabetes possibly related to her hepatitis C. We now know that if we identify patients early and treat them, at least in some instances

we will be able to entirely prevent those complications.

MR. BUSKER: And finally: the management priorities in patients with extrahepatic manifestations and the impact of hepatitis C eradication.

DR. FELD: I think all of our cases highlighted the importance of eradicating the viral infection, so hepatitis C antiviral therapy to prevent further disease progression and establish a durable virological cure. The other point was that in some instances additional therapy beyond antiviral treatment is required; for example, immunologic therapy for cryoglobulinemia and chemotherapy for high grade lymphoma. The virological cure is still a mainstay of treatment of all extrahepatic manifestations of hepatitis C.

MR. BUSKER: From the University of Toronto, Dr. Jordan Feld, Dr. Joel Emery, thank you both for participating in this eViralHepatitis Review Podcast.

DR. FELD: Thanks a lot, Bob, I enjoyed the discussion with some great cases and some good, challenging conversation.

DR. EMERY: It's been my pleasure, Bob, thank you.

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 eViralHepatitis 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 eViralHepatitis Review via email, please go to our website: www.eviralhepatitisreview.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.

eViralHepatitis 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.

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.