

Hepatitis C and COVID-19: What Clinicians in Rural and Underserved Areas Need to Know

Transcript

Voiceover: Welcome to this CME activity, *Hepatitis C and COVID-19: What Clinicians in Rural and Underserved Areas Need to Know*. This activity has been planned and implemented by RME Collaborative and Boston University School of Medicine.

The faculty for this program are Dr. Barbara Yawn and Dr. Nancy Reau. Dr. Yawn is a rural family medicine physician and adjunct professor at the University of Minnesota. Dr. Reau is a Professor of Medicine at Rush Medical College and the Section Chief of Hepatology and Associate Director of Organ Transplantation at Rush University Medical Center in Illinois.

Barbara P. Yawn, MD: Well, let's begin, but first I want to remind our listeners that we are recording this podcast on July 7, 2020, and the information about COVID-19 continues to evolve as we learn more about the virus day to day.

So, Nancy, can you start off by giving our listeners an overview of how liver disease management in general has changed since the COVID-19 pandemic started?

Nancy S. Reau, MD: Yeah, I think that most people have definitely felt their lives disrupted by COVID-19. And in healthcare, everything came to a screeching standstill while we tried to make sure that the healthcare system could keep people safe while still maintaining some ability to care for the COVID-19 patients. And that meant that everything routine essentially disappeared.

We suspect that as we try to bring that back, like so, re-entry is no smoother in healthcare than it has been in other forms of re-entry like restaurants and going back to school. Our medical system is now trying their best to bring things that are urgent or that really need to have management back in safely while still managing the COVID-19 patients, but have not necessarily disappeared.

There's a really interesting article by Elliot Tapper that looked at some of the stages of this disruption. And the first is the most obvious one – things shut down and nothing happens, nothing happens except for the absolute emergent. And when you even think of the absolute emergent, there are studies showing that with acute coronary syndrome, people were not coming into the hospital. They're afraid. And so, if you're not coming during a heart attack, you're probably not going to come when you might have a sign of liver disease.

After that, when things start to reopen, there's this huge attempt to get the things that we didn't do done at the same time as the things that we're supposed to be doing right now. So, you can imagine that all of the appointments from March, April, May that were deferred until August didn't mean the patients that were going to come into the system in August, September, and October aren't there. We're trying to do two things at once. We'll still be social distancing, so you're supposed to be doing less, but we're actually trying to do double.

And that's pushing out a lot of the screening and surveillance that we should be doing to a time where in phase three you're going to have emergencies occur that could have been prevented because we're not able to get the patients into the system to do the basic preventive care. And then that increases things

like cancer and chronic diseases that really should have had better management and now are poorly managed.

Barbara P. Yawn, MD: It is going to be a real concern because we also have all of the depression and addiction and all those other issues on top of the chronic health issues like liver disease or diabetes or whatever that both the patients and the healthcare system and healthcare professionals are going to have to put up with.

So, Nancy, in addition to all of the other things happening, sort of at the same time there were some really quite remarkable changes in the recommendations for screening for hepatitis C. Can you review those with us, tell us what they are and why they changed?

Nancy S. Reau, MD: So, we were really pretty excited with the changes that even recruited screening for the birth cohort, people born between 1945 and 1965, which were enriched with hepatitis C and actually had more concentrated, advanced disease. These are individuals that had been living with hep C longer.

But, the opioid epidemic has led to a lot of hepatitis C transmission in a much younger cohort and we knew that the guidelines had to change. And luckily CDC in the United States invented a task force and the individual liver societies and GI societies have all agreed upon these much more broad screenings. And now it's recommended that all individuals between the age of 18 and 79 have at least a one-time screen. And if you have risk factors, so someone that has addiction or IV drug use or other high-risk factors, there is now recommendation for ongoing screening. And these are not age based or – you know, the birth cohort is still important. But this significantly expands our screening opportunities.

Barbara P. Yawn, MD: And during pregnancy do we do additional screening or somebody's been screened once and then they get pregnant three years later, they don't have to be screened?

Nancy S. Reau, MD: So, I think that this is a place there has been some controversy. Our guidelines now recommend hepatitis C screening in all pregnant women and if you interpret this more broadly that would be with each pregnancy irrespective of what you might have screened in the past.

I don't think that this is because hepatitis C transmission during pregnancy is significantly high. Luckily, hep C rarely is transmitted to the infant at the time of birth. It's just a great opportunity to identify a young cohort at a time where they might have a stable period in their life and so the opportunity to identify individuals who are interacting with the healthcare system when they may not have, is a great time for screening.

Barbara P. Yawn, MD: Yeah. I think that's always important – is if you've got them, screen them. Or if you've got them, immunize them. So, that's important.

I wonder have there been any other updates in the guidelines, like for treatment?

Nancy S. Reau, MD: Well, our guidelines used to be pretty heavy-handed. They were always a great roadmap for what therapy might match to the patient characteristics. But now our guidelines have included a very simplistic algorithm to allow less sophisticated proprietors to give hepatitis C care.

As you look at the population with hep C, most individuals are treatment naïve, not cirrhotic. They're young. So, they in theory should be a very easy to treat group of individuals from a disease standpoint.

Now, they might have psychosocial factors that make engaging the medical system a little bit more challenging. But, curing their hep C if you can get them access to drugs and they take the drugs, it's pretty low-hanging fruit, very simple. And because of that, the guidelines have given you this nice algorithm that is very easy to help walk someone through taking care of those patients. It really requires them to look for fibrosis. You never want to miss someone who's got more advanced disease. Make sure the individual is not co-infected with HIV or hepatitis B. These do add significant risk. Make sure you're doing that drug/drug interaction view so that many of the medications that you get for opioid addiction are very easy to integrate into hep C therapy. But, you want to make sure you look at the medications just so you don't run into toxicity or less efficacy of the therapy.

And then as long as those like pretty simplistic rules are in place, patient characteristics are in place, there are great very simple pan-genotypic treatments that are, you know, one pill a day or pills once a day for eight to twelve weeks. And the chance for a cure is a hundred percent if the patient takes medicines appropriately. And that leads to very minimal on-treatment monitoring. You really just have to document cure at the end of the course. And that should allow us to imbed hep C treatment in addiction services; allow us to use alternative models such as nurse-based models or APP-based models; allow family doctors or rural physicians with or without mentoring, when they become more experienced, to really do hepatitis C treatment, so that patients don't have to go through that laborious effort of going to an academic center or finding that one GI specialist a hundred miles away that's capable or interested in treating hepatitis C.

So, I think that not only has screening become much more broad-based, but the understanding that we've got to change the traditional model of hepatitis C treatment in order to get patients to navigate that cascade of care is incredibly important.

Barbara P. Yawn, MD: I agree. I remember when hepatitis C treatment first became available, it was quite complex, and there were all kinds of concerns about co-morbid conditions, some of them being the most common co-morbid conditions, kept you from getting help for your hepatitis C treatment. So, I'm very excited about that.

And to help people see the algorithm that you talked about, Nancy, we're going to display it on the activity page, so you'll be able to find the link to that and the algorithm for you to decide how to incorporate into your practice.

One of the things that we haven't talked about though is acute hepatitis C infection. How do you know someone has an acute infection? And are there recommendations for acute management?

Nancy S. Reau, MD: Yeah, so, that's a great question because hepatitis C is traditionally either asymptomatic or has symptoms that are not very specific to liver disease.

And so a lot of individuals that get acutely infected might feel fatigue or a little, you know, flu-like symptoms but have no idea this is viral hepatitis. And someone who's acutely infected might run the risk of transmitting. And so our guidelines now are pretty open in encouraging individuals who have acute infection to actually engage in treatment. That's a change. Because we know that spontaneous clearance is true and up to a third of individuals, especially younger individuals or symptomatic individuals. Now taking that period of time where we're waiting for them to spontaneously clear, especially if they're engaged in high-risk practices, means that they're going to transmit the virus.

So now, we treat them just like you would someone who's got chronic infection. There are studies that show a very short duration treatment might work. But our guidelines really still now recommend a full course of therapy. Remember, treatment is usually just eight to twelve weeks, just to make sure that we have appropriately characterized the patient and given them the best opportunity for cure.

Most of our acute infections, though, are found through surveillance programs. If you have someone who is, you know, an IV drug user or in a methadone program, a lot of these programs are screening their individuals with high-risk factors on a regular basis, as our guidelines recommend for hepatitis C.

And so we find a lot of asymptomatic infections that way in someone who has newly become hepatitis C positive.

Barbara P. Yawn, MD: We know that the treatment for hepatitis C has really evolved tremendously over the past decade. What therapies are now available? And how have they changed the way we approach treatment today?

Nancy S. Reau, MD: So, we have seen a significant evolution in our treatments starting from things that were very complicated, injection therapy, a lot of pills. And now we are really down to four all-oral treatments. We have two pan-genotypic therapies, that means that the same regimen is appropriate regardless of the patient's genotype. And that's GP or glecaprevir/pibrentasvir or SOF/VEL, which is sofosbuvir and velpatasvir, which also has a generic form.

We have two therapies that are still used a little bit. They are not pan-genotypic, so this requires an additional step in your algorithm. You have to know the patient's genotype. They're still very effective when used appropriately. That's elbasvir and grazoprevir and then ledipasvir and sofosbuvir, which was our first oral treatment.

And it doesn't really matter which of these therapies are used for the patient. They all have incredibly high efficacy as long as you make sure you either use a pan-genotypic one, or if you're going to use something that genotype specific, that you know the patient's genotype.

Barbara P. Yawn, MD: And do we have to worry that people may have more than one genotype? Or does someone who's infected almost always have a single genotype?

Nancy S. Reau, MD: Yeah, so our diagnostics are usually not sensitive enough to find multiple genotypes. But if you're using a pan-genotypic therapy, then that gives you that assurance that even if you had a patient who was characterized as genotype 1 but had a small subset of genotype 3 in there, remember a lot of our IV drug users have had multiple exposures to hepatitis C and could have multiple genotypes in their body even if not detected by the lab. Pan-genotypic therapy gives us the ability to not have to worry about that.

We do find that sometimes this is a really important thing to remember. If you've given someone something that's specific for genotype 1 and then they have hepatitis C after therapy and it's genotype 3, lots of times we are accusatory or think that they've been re-infected. And there have been times where we go back and look at their original blood, you know, send it off for more specific testing. And we've found that they had genotype 3 there anyway and the therapy you gave them wasn't effective enough.

So, reinfection still is the most common explanation in that group of individuals, but it's not the only one.

Barbara P. Yawn, MD: So, it sounds like it's very important to think about that and for example, someone who may have had potential exposures over a long period of time and has maybe been exposed multiple times, you really want to think about this.

Are insurances covering most of the therapies?

Nancy S. Reau, MD: So, there is variability in coverage based on what state you're practicing in, which type of insurance your patient has. But, at least in Illinois we had some pretty radical changes in access. They eliminated fibrosis and substance abuse restrictions. And that really has given us a pretty permissive system to get hepatitis C treatment to all of our patients.

Our companies have some great programs for those that are uninsured or have you know, insurance that does not cover drug privileges. And there are a lot of patient access programs that you know, even if an altruistic program through one of the drug companies is not available, we often have other ways of getting help with hepatitis C treatment.

Remember, we do also have two generics. And so, when you have this number of opportunities for the patients in front of us, even though therapy is still expensive, it's rare that I can't get access now because of insurance limitations for my patients.

Barbara P. Yawn, MD: Well, and this is one of the reasons, another one of the reasons, sometimes we really do ask for our friendly hepatology or GI colleagues to help us out with these people. You may have more experience and resources to help us identify support or treatment than we may.

Do we have to worry about are these – they're all pills now, which is really helpful. But, multiple times a day with food or without? Are there ones we should watch out with, say, kidney disease or something like that?

Nancy S. Reau, MD: Yeah, so the treatment used to be incredibly complicated. There are still some things you need to be aware of, and I think that drug/drug interactions are one of the most important. Some of our treatments really need to have some awareness around acid suppression or seizure medicines. But, for the most part these are, you know, once a day therapies, all pills. They're getting pediatric indications so that really kind of emphasizes the safety. Glecaprevir/pibrentasvir does still require it be taken not on an empty stomach, with food, so that's different. The others don't require any kind of food to be taken, you can be fasting or not fasting.

And we used to know that sofosbuvir had some poor clearance with at least a metabolite of sofosbuvir in those with more advanced kidney disease. But, our guidelines have recently opened that up as that did not appear to be toxic, it was just a metabolite that needed to have more investigation.

So that for the most part, very few characteristics of the patient are going to change which therapy is going to allow them to be cured. Once, you get that treatment, though, it's really important to explain to the patient how they're going to take it, as glecaprevir/pibrentasvir is once a day therapy for eight weeks. Sofosbuvir/velpatasvir is one pill a day for twelve weeks. And so, if we have counseled our patient wrong we don't want to see them either not, you know, not taking their treatment correctly because they thought they had the other therapy.

Barbara P. Yawn, MD: And those are important issues. But it sounds like we have a treatment that is very appropriate now to consider widespread, including in primary care. So, from your perspective, what is the role of primary care clinicians in hepatitis C treatment and management?

Nancy S. Reau, MD: I think primary care has a very important role here. We recognize that along the care cascade, that there's a huge drop-off from screening to diagnosis to linkage to care.

Now, from screening to diagnosis, we have an antibody that can automatically reflex to a PCR so that eliminates the two steps that used to be required for antibody positivity that the patient had to come back and then get a viral load drawn. So, you can identify easily a person who's infected. But, that second step now – getting that individual linked to someone who can offer them therapy, is where a lot of patients just disappear.

We know from multiple models that if you can keep all of that in their medical home, they're much more likely to get access to treatment because they don't have to establish with another provider.

So, I think that our primary care doctors, when they're interested in hepatitis C treatment and they have the security that they can do that safely, and they have a mentoring relationship so when they have questions they can easily reach out, I think that primary care will ultimately treat the majority of hepatitis C.

Now, as long as you have access to someone like a tertiary care center or someone that has subspecialty management, we try to encourage our primary care providers to not, you know, treat co-infection with HIV or certainly not a decompensated cirrhotic. These individuals are more, you know, higher risk and either need that infectious disease support or a hepatologist to even talk about is treatment appropriate, is this person more appropriate for transplant?

We also like embedded addiction services. So sometimes, it's not the hepatitis C that's the biggest limitation. It's getting that individual linked to, you know, methadone treatment or something that can help them with their addiction and stability. That's the most important way of getting their hepatitis C cured.

Barbara P. Yawn, MD: Well, you mentioned mentorship and helping and you know, I think there are many rural, especially primary care physicians, who realize this important need and are very – we're very aware that if we send someone 180 miles away, it falls off. A significant proportion won't go. But the first time I do this or the first three or four or five times I do this, it might be nice to have some mentoring. And how do I do that if I don't have an established relationship already?

Nancy S. Reau, MD: Yeah, so here I know there are a number of existing programs that can link a mentor or a teaching facility with an individual who's interested in hepatitis C treatment. ECHO is probably one of the most well-known. But CDC has opportunities, there is something called HepCAP. A lot of times your local university or who you might refer a patient who's got advanced disease – the individuals in there might be very happy to give you their cell phone number so that you can reach out.

In our own program, we have a training program for our internal medicine residents and our family practice residents. So, they are starting to treat hepatitis C themselves in the residency. And then when they, you know, get jobs in the community, in rural Illinois or wherever they end up, we hope to have already given them the confidence to treat hepatitis C and then they can be a mentor for their own

partners. Plus, when you're trained, you know, your mentors at your own training situation, they're usually pretty readily available to you even after you graduate.

So, there are established models. There are lots of ways to be creative for individuals to, you know, seek out someone who can kind of hold their hand a little bit when they have questions.

Barbara P. Yawn, MD: I think it's really important that we have those mentoring programs, and I'm so excited to hear about them. When we talk about that, are there things for monitoring and follow-up testing that we need to think about?

Nancy S. Reau, MD: Yeah, so I think the simplified algorithms have really made on-treatment monitoring pretty easy. When you read through all the texts and the guidelines, some patients might still like to have labs at one month to make sure that they've cleared, give them the encouragement that they're doing the right thing.

But, you know, in reality you can really prescribe the medications as long as there isn't something that needs to be monitored, like a drug/drug interaction, and expect after eight to twelve weeks of compliance that the patient has not you know, should not have any side effects, should not have any kind of lab abnormality that needed to have on-treatment monitoring and should have achieved a cure, that you just need to verify three months later.

So, these simplified algorithms in a low complexity patient really allow very minimal touch points.

Now, it's important to recognize that some patients need the touch points, not necessarily to make sure their hep C treatment is effective and safe, but rather because they need that support of whether it's for food safety or for addiction management or just, you know, for their psychosocial wellbeing, to know that they're on track and doing the right thing. We don't neglect our patients. Some we find really need the phone calls, they enjoy talking to our nurse or to their physician through their course of treatment. It's just not necessary and should not be a hindrance to providing treatment to the bulk of your patients.

Barbara P. Yawn, MD: I think that's really important. The ongoing management is always really important.

What about hepatitis C and coronavirus? Are there any special things you tell the patients, special precautions?

Nancy S. Reau, MD: Yes, so here I think we have two things. The first is that studies have hands down suggested that having hepatitis C without advanced liver disease does not increase your risk of either getting COVID-19 or of having an outcome different than the general population.

So, if you have hepatitis C, you shouldn't be afraid that you are going to have a worse outcome but certainly still social distance, take all your precautions. You know, I think that's important for all people across the board irrespective of their viral status.

The second is that telemedicine or some of these alternative models that can allow us to still operate at some semblance of normalcy without bringing our patients into a tertiary care center that might run the risk of exposure has really helped considerably for hepatitis C. In my own practice, if we have a referral for hep C treatment, you know, so someone who's diagnosed with hepatitis C and referred for that linkage to care, I will have my pharmacist actually secure treatment and I'll get all the labs I need in

order to do the precertification before the patient comes to clinic so that one opportunity when I'm needing those, I can actually send them home with their drug or, you know, talk to them about how they're going to initiate treatment so that they don't have to repeatedly come in and out of the medical system.

In some patients, especially those that have a primary care provider that has referred and is very involved, we may not see the patient in person at all. We might do everything through telehealth. This has really allowed us to facilitate treatment at a time when we're trying to keep people out of the medical system but still keep on track for those WHO elimination goals by 2030.

Barbara P. Yawn, MD: It sounds like this is an appropriate opportunity for telehealth since most of the follow-up can be done without having to come in for labs or other things. So, very exciting.

Can you give us your three take-home messages from today, please?

Nancy S. Reau, MD: Yeah, so I think that one of the most important things is to remember in this pandemic era – social distance. A lot of our hepatitis C patients or individuals at risk for hepatitis C are struggling with addiction, depression, social isolation. So, finding the services is important but still wearing your mask and making sure you wash your hands, don't place yourself at risk that's unneeded.

The second is vaccination. We can really blunt the flu symptoms if we can prevent flu. If you're going to get COVID-19, you want to be able to recognize it. So, get your flu and Pneumovax, so that you don't have you know, exposure to a similar presentation, so that it's much easier to identify those that do get exposed to SARS-COV-2.

And then the last is you know, continue to, you know, not be afraid of the medical system but use it creatively. That means you work with your doctor if you're a patient. You use telehealth or find a way of getting appropriate care without becoming unsafe. Use your community labs, your local hospital imaging. Find a way to navigate the healthcare system. Don't neglect your health so that we don't find that healthcare really has taken a huge toll on routine management that could have prevented a lot of more complex disease.

Barbara P. Yawn, MD: Thank you so much. And I do want to remind people that we do have links to some of the support and available mentoring kinds of services and that's on the activities page.

So, Nancy, Dr. Reau, thank you so much for sharing your insights and helping us better understand how to manage hepatitis C infection in this era of COVID-19.

To our listeners, please remember to complete the program evaluation to receive CME/CE credit.

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