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Addressing Treatment Challenges in Hepatitis D Patients

Dr. Buch:

According to the CDC, delta hepatitis, or hepatitis D, is a liver infection that only occurs in people who are also infected with hepatitis B. So what do w need to know about hepatitis D?

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And today we are joined by Dr. Robert Wong who is the lead author of "Lov Performance of Hepatitis Delta Virus Testing Among Two National Cohorts of Chronic Hepatitis B Patients in the United States," which was published i the *American Journal of Gastroenterology* in 2022. Dr. Wong is a Clinical Associate Professor at Stanford University.

Dr. Wong, Welcome back to the program.

Dr. Wong:
Hi, Dr. Buch. Thank you for having me.

Dr. Buch:
It's a pleasure having you join us today. So let's start with some background, Dr. Wong. Why does hepatitis D only exist in patients with the hepatitis virus?

Dr. Wong:
Fantastic. That's a really great question to start because it emphasizes the importance of thinking about hepatitis delta in the context of having chroni hepatitis B. Hepatitis delta virus is in some ways a defective virus, and the reason it requires having the presence or concurrent infection with hepatitis B i that the delta virus utilizes the machinery or the replication potential of hepatitis B to multiply, replicate, and develop its complications associated with live disease throughout an individual's system, so in that sense it's important to think about these two viruses in conjunction with each other. But that's th main point is that hepatitis delta occurs only in the setting of hepatitis B because it utilizes its replication network to multiply.

Dr. Buch:
And when should we be concerned that a patient might have hepatitis D or delta?

Dr. Wong:
So when thinking about who to screen or who might be infected with hepatitis delta, it's actually a little bit of a challenging question. There are differer guidelines and different societies that have different recommendations. For example, the European Association for Study of Liver Disease and the Asia Pacific Association both recommend testing all patients with chronic hepatitis B for delta superinfection. However, in the U.S., the current version of th AASLD guidelines recommend testing only in patients with certain risk factors, and these include patients that are from high-risk or high-prevalence region for hepatitis delta; those with certain risk factors, such as IV drug use, HIV coinfection, hep C coinfection; or in the clinical context when things don't mak sense or may suggest an alternative diagnosis to purely having only chronic hepatitis B. As you can see, that creates a little bit of confusion, and perhaps

inconsistency in who to evaluate for hepatitis delta testing. There are some thoughts that the U.S. guidelines may be updated soon to simplify th approach, and also recommend testing all patients. I think that's going to be an important update to the guidelines. By recommending testing all patients not only simplifies the approach, but it raises awareness, and also reduces the potential stigma associated with identifying who has or does not have ris factors for delta testing.

Dr. Buch:
And, Dr. Wong, as a follow-up to that, if we test all patients with hepatitis B for delta hepatitis, is there any downside?

Dr. Wong:
There's no downside from a clinical aspect. In fact, there is benefit in early detection, linkage to care, and treatment to reduce the risk of diseas progression and liver disease complications. However, there may be some concerns about cost-effectiveness and healthcare resource utilization. Whil there have been studies looking at and showing that one-time testing for hepatitis B is cost-effective, currently, there are no data specifically looking at cos effectiveness of testing for delta. Nevertheless, there is abundance of data showing that early testing and detection and reducing long-term risk of live disease progression is an appropriate and beneficial path to take to reduce patient morbidity and mortality.

Dr. Buch:
Thank you for that. And let's go into definitions a little bit, which are really important clinically. What's the difference between hepatitis B and delt coinfection versus hepatitis delta superinfection?

Dr. Wong:
It's important to think about these different terminologies because it reflects the natural history or the route of infection. Typically, most patients that hav delta infection have underlying hepatitis, chronic hepatitis B, and for whatever reason, whether it's risk factor or something else, they acquire delta infectio on top of chronic hepatitis B, so we think of that as superinfection, meaning they have had chronic hep B and then they now acquire an additional infectio on top of that. When we say coinfection, we really just mean that someone gets infected with hepatitis B and delta at the same time.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Robert Wong about patients wh present with delta hepatitis, or hepatitis D.

Switching gears a bit, Dr. Wong, can you tell us about the effectiveness of the hepatitis B vaccines in preventing delta hepatitis?

Dr. Wong:
Yeah, that's a really great question, and I'm glad you brought this up. Hepatitis B vaccinations are very effective because the hepatitis B vaccinatio prevents someone from developing chronic hepatitis B. And as we discussed a little bit earlier, hepatitis delta really requires having underlying hepatitis I virus to replicate and multiply, and so by corollary, if someone is vaccinated for hepatitis B, by preventing hepatitis B, they are therefore, preventing hepatit delta. And this is particularly a relevant topic to emphasize for your listeners because, as many of you know, there has been a recent update to th recommendations for hepatitis B vaccination, such that the CDC is now recommending vaccinating all the adults age 18–59 for hepatitis B, and the vaccinating those 60 and above with risk factors, so it really is a call for renewed awareness about ensuring that we provide and implement effectiv screening followed by vaccination for hepatitis B.

Dr. Buch:
So with that in mind, what are the treatments that are available for delta hepatitis patients?

Dr. Wong:
That's another great question. Hepatitis delta is very deadly. In fact, some say it's the most deadly hepatitis virus out there because it's associated wit very high rates of disease progression to cirrhosis, HCC liver cancer, and mortality. Unfortunately, currently, in the U.S. there is no FDA-approved therap specifically for hepatitis delta. For many years, we've used pegylated interferon off-label, and pegylated interferon is associated with many side effects, ar also does not achieve very high rates of successful viral suppression. But there are very promising therapies just on the horizon. The most promising on that it's near is called bulevirtide, or also called Myrcludex. This has been conditionally approved and available in certain European countries, so it is i use. In the U.S. it is currently undergoing review, and we hope that it will soon be available later on this year.

There are some other investigational therapies that are also far along, and these include lonafarnib. It's a farnesylation inhibitor. And then there are othe formulations of interferon, one called interferon lambda, which is a different formulation that tries to maximize the benefit by improving the targeted effect c interferon in limiting some of the associated side effects that have really made using interferon so challenging in the past.

Dr. Buch:
As a continuation to that thought, are there any differences in effectiveness of these medicines among the eight genotypes of delta hepatitis?

Dr. Wong:
Yeah, that's another fascinating question. So we learned early on from hepatitis C that at least in the early days there were some differences i effectiveness of antivirals, depending on the genotype. Hepatitis B and hepatitis delta have different genotypes. To the best of our knowledge, currentl there is no differences in effectiveness of therapies across the different genotypes of delta or hepatitis B. Now part of that is probably we have nc developed targeted therapies. The other part of it is we don't routinely check genotype for hepatitis B or hepatitis delta. And currently, the genotype c both of these does not really affect our clinical management. As far as we know, there's no difference in effectiveness of antiviral therapies for thes different disease states, but I suspect that as treatment and as our understanding of these viruses evolve, similar to hepatitis C, we may have targe therapies that are individualized or personalized to specific virus and patient characteristics in the future.

Dr. Buch:
This has been an informative discussion about delta hepatitis. I want to thank my guest, Dr. Robert Wong, for an excellent discussion. Thanks very muc for joining us today.

Dr. Wong:
Thank you so much for having me.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of th Knowledge. Thanks for listening and see you next time.