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How Improved Hepatitis B Vaccination Coverage Can Protect At-Risk Adults

ANNOUNCER: Welcome to CME on ReachMD. This activity, entitled "How Improved Hepatitis B Vaccination Coverage Can Protect At-Risk Adult" is provided by the National Foundation for Infectious Diseases (NFID) and supported through an unrestricted educational grant from Dynavax Technologies Corporation. [NFID policies](#) restrict funders from controlling program content.

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Here's your host, Dr. William Schaffner.

DR. WILLIAM SCHAFFNER: Hepatitis B vaccines are safe and effective, yet only about 25% of U.S. adults are vaccinated against hepatitis B virus, HBV, as recommended. Those who remain unimmunized are at risk for acute HBV infection, which can progress to chronic infection, which can lead to cirrhosis, liver cancer, and death. Improved hepatitis B vaccination coverage rates in U.S. adults can help slow the rate of acute infections and reduce the reservoir of infections.

This is CME on ReachMD, and I'm Dr. Bill Schaffner, Medical Director of the National Foundation for Infectious Diseases and Professor of Infectious Diseases at the Vanderbilt University Medical Center. Joining me for today's program, focusing on hepatitis B vaccination, is my good friend, Dr. Arthur Reingold, who is Professor of Epidemiology in the School of Public Health at the University of California Berkeley.

Art, thank you for being here today.

DR. ART REINGOLD: I'm happy to be here, it's a pleasure.

DR. SCHAFFNER: So, Art, we know the rate of reported cases of acute HBV infection in the U.S. declined nearly 90% following the widespread uptake of hepatitis B vaccine in infants when it was made part of the routine immunization schedule. So, where does that leave us today? Can you tell us what the current data show regarding the burden of HBV infection in the United States?

DR. REINGOLD: Sure, I'd be happy to. I think it's important to point out, as you have already indicated, that because we made the infant immunization with hepatitis B vaccine a regular feature of the infant immunization schedule in 1991, 25 years ago, we really have very little in the way of hepatitis B infections in infants and children at this point, and that's the good news. It has resulted in a sharp decline in the incidence of acute hepatitis B virus infections in the United States, but unfortunately, we haven't been quite as able to deal with acute hepatitis B infections in adults, and so most of the burden now in the United States of HBV infection is, in fact, in adults, particularly those 30-59 years of age.

CDC has estimated – well actually, based on reports in 2016, there were a little over 3,200 acute hepatitis B virus infections reported in the U.S., again overwhelmingly in adults, but of course because of a lot of these infections are asymptomatic and go unreported, the estimate is that there could be as many as 21,000 HBV infections annually in the United States. Now, it is also important to point out that, while many of these acute infections are asymptomatic or produce a self-limited illness in adults, a very small percentage of acutely infected adults will have a very severe illness with occasional death, but the bigger problem, frankly, is that about 5% of those adults will go on to develop chronic hepatitis B infection; many of them not aware they're infected, and they contribute to ongoing

transmission. Again, based on CDC estimates and surveys, there may be as many as 2.2 million individuals with chronic hepatitis B virus infection in the United States. And those individuals that are chronically infected, are at substantially increased risk for some really bad things happening to them with regards to chronic liver disease, so they're at increased risk of cirrhosis of the liver, hepatocellular carcinoma, and liver failure. We estimate that about one in four individuals with chronic hepatitis B virus infection will die prematurely as a result of these complications.

DR. SCHAFFNER: You've certainly described a substantial burden of both acute and chronic hepatitis B virus related disease. Why don't you remind us on how the hepatitis B virus is spread?

DR. REINGOLD: The hepatitis B virus is a DNA virus. And it's primarily transmitted through contact with blood or other bodily fluids, such as sexual fluids if you will. And basically, to be transmitted quite readily to blood contact or percutaneous exposure to blood or through sexual contact, though there does not need to be visible blood present. It can certainly be transmitted in the absence of visible blood. And while we're not talking here today mostly about the mother-child transmission, that is also a phenomenon that hepatitis B virus can be fairly readily transmitted from an infected woman to her newborn baby. It's important to point out that hepatitis B virus is extremely infectious when it's in blood and other body fluids; probably in the range of 50-100 times more infectious than human immunodeficiency virus. Furthermore, it's a fairly hearty virus. So, if it gets onto a surface such as in a dialysis center, or something for testing diabetics for their blood sugar or something like that, it can remain infectious outside the body for at least a week. So, it doesn't become inactivated quickly once it's outside the body. So again, in the United States, the primary routes of transmission among adults at this point are through percutaneous exposure. For example, injection drug use is a very common way in which it is transmitted, and also sexual contact; either heterosexual contact or sex among men who have sex with men. Those would really be the two most common routes of exposure in adults in the United States.

DR. SCHAFFNER: Now, Art, hepatitis B is sometimes called "a silent killer." Let's talk about how the disease earns that particular ominous reputation.

DR. REINGOLD: Well, of course, in some ways in that respect it's similar to hepatitis C and HIV infections in that many of the initial infections are totally asymptomatic. So, we estimate about half, about 50% of adults who contract hepatitis B virus infection will be completely asymptomatic, so they won't know that they've acquired it, particularly if they become chronically infected, they can then go on to transmit others around them not knowing they're infected and not knowing that they're transmitting. Furthermore, in such individuals, the replication of the virus can continue for decades among such individuals, so the virus is replicating and maybe doing damage to the liver in that individual, and that individual can readily be a source of infection to others. So, the best guess is that about two-thirds of those with chronic hepatitis B virus infection do not know they're infected, and obviously if they don't know they're infected, they may not take precautions in terms of transmitting the virus to others. And they themselves, because they don't know they're infected, are potentially not going to find out until the virus has caused severe liver damage years later, at which point, either because of fibrosis of the liver or cirrhosis or cancer of the liver, they will have substantially increased morbidity and mortality.

DR. SCHAFFNER: So, it's not only a silent killer, they can be silent transmitters, which brings us to prevention. So, let's focus on vaccination efforts. First, can you talk about the patients for whom hepatitis B vaccination is recommended, what risk factors should we be aware of as we think about vaccinating our patients?

DR. REINGOLD: Again, where it's not the focus today, but certainly in addition to routine recommendations that all infants receive hepatitis B vaccine preferably the first dose even before leaving the hospital within 24 hours of birth, we also want to ensure that all pregnant women are screened. Leaving aside infants and pregnant women, focusing on other adults, the ACIP, the Advisory Committee on Immunization Practices, does have recommendations for hepatitis B vaccination for adults in certain categories. One of those categories, of course, is healthcare workers. Healthcare workers are certainly a strong focus of hepatitis B vaccination and, while those workers have been increasingly receiving vaccines, the levels of vaccination in healthcare workers is still frankly below what we would like them to be.

Secondly, we want individuals at risk of sexual exposure to the virus to receive the vaccine. And we can talk about settings in which that can take place, but for example, patients being seen in an STD clinic are at high risk of hepatitis B virus infection. So, the vaccine should certainly be recommended in individuals at risk from sexual exposure, including quite a few men who have sex with men, who may be having multiple partners. We clearly would like to also identify those who are at increased risk from exposure to contaminated blood, and that again certainly includes healthcare workers, but it also includes people who inject drugs, it includes first responders such as people who are driving ambulances and responding to people who are ill out in the community and may have exposures to blood. And then, in addition, we want to identify for vaccination people either with certain existing health conditions such as on hemodialysis or with diabetes. We want to identify people who have certain living situations that increase their risk of hepatitis B infection, and that would include people living in the household with someone known to be infected with hepatitis B virus. And then we want to also make the

vaccine available and then hopefully get people to take it if their travel plans will take them to a country where hepatitis B virus infection is endemic and much more common, even though there are risks of getting infected that will primarily depend on percutaneous exposures and sexual activity, the fact is, if you are traveling in a country with a high prevalence of hepatitis B virus infection, you would be well advised to receive hepatitis B vaccine before you travel. Back in 1982, that's why I receive the vaccine, because I was doing quite a bit of work in West Africa and in Asia in settings where the virus was quite common. So those are the three groups that we particularly want to target, and then of course we want to make the vaccine available to any adult who wants to be protected against this infection. So, any patient who requests the vaccine, should be given it. It is not necessary to take a risk factor history, although in the clinical setting, that could certainly be helpful to the provider in ascertaining who might benefit from the vaccine. But if a patient comes in and says, 'I'd like to be protected against hepatitis B virus,' then we should be making sure that they receive the vaccine, as well. So those are the primary groups. There's not currently universal recommendation that all adults in the United States receive hepatitis B vaccine, so we have these specific groups we are attempting to target.

DR. SCHAFFNER: So, you know, when I give medical grand-rounds on this topic, there are two groups that usually surprise my audiences. So, let me call them out, and I invite your brief comment. The first has to do with sexual exposure. So, if you have multiple partners, even if they're serial multiple partners – you know, you're a serial monogamist as they're called – and certainly if you are not in any way monogamous, you ought to get hepatitis B vaccine. So that's one group. They encompass a very large proportion of young adults. The second is diabetes. I think it was in late 2010 that the CDC's Advisory Committee on Immunization Practices recommended that everyone with diabetes get vaccinated against hepatitis B as quickly as possible after their initial diagnosis. Those two recommendations usually come as a bit of a surprise to a lot of the practitioners, internists, family doctors, and others who are in my audiences. Do you care to comment?

DR. REINGOLD: So, with regards to diabetics, I think there are a couple of reasons historically why that recommendation was made. First of all, obviously, many diabetics, if not most diabetics undergo fairly frequent testing for their blood sugar, and some of the devices that have been used in the past to obtain that blood sample, unfortunately, have contributed to the transmission of blood-borne viruses such as hepatitis B virus. So, some of this relates to increased exposure through that route, at least historically. Also, the fact that the people when they have more advanced diabetes after they have for a lengthy period of time, may not respond quite as robustly to the vaccine so if we're going to vaccinate, then vaccinating them earlier in the course of their diabetes is likely to give them protection sooner and there will be a more robust immune response. People who are sexually active and having multiple partners either concurrently or serially are certainly a group we would like to protect. I think you're right that many people perceive if they are serially monogamous, that somehow that doesn't include them, but because many people are not aware of their hepatitis B virus infection status, you can easily have a sexual partner who is infected and he or she doesn't know they're infected. So, I think you're right that patients and providers may not fully see why those individuals are targeted, but they certainly are at some risk and we would like to prevent infection in them.

DR. SCHAFFNER: We've now talked about the sorts of people who ought to be vaccinated, who ought to receive the vaccines. Say a few words about actually which vaccines are licensed for use in adults in the U.S. and how effective are they?

DR. REINGOLD: Well, I'd say first of all the good news is that we have a number of hepatitis B vaccines and they're both highly effective and quite safe, so we now have several decades of experience with them. Historically, there were two single-antigen hepatitis B vaccines, but recently a third has been added, so we have three single-antigen hepatitis B vaccines licensed for use in adults in the United States. And then we also have a vaccine that combines hepatitis A and hepatitis B vaccine, which is licensed for use in the United States and is particularly helpful in terms of potentially people traveling overseas. So, the two longer-standing vaccines, if you will, are Energix-B® and Recombivax HB®. The more newly-licensed vaccine, which we just licensed in November 2017 is Heplisav-B®. So, the two older vaccines are typically administered as a three-dose schedule, and the newer vaccine, which was designed really to be more immunogenic is licensed as a two-dose series. There are alternative dosing schedules and special formulations for specific patient groups and for accelerated protection, but fundamentally we have a range of options from hepatitis B vaccines and, certainly with the two older vaccines we now have experience delivering them to millions and millions of people.

So, we also have very good data, not only about their efficacy and immunogenicity, but about their safety. And the safety data are, I would say, very, very reassuring. Of course, like any injectable vaccine, there can be pain at the injection site, there can be fever, there is an association between receiving hepatitis B vaccine and anaphylaxis at least in yeast-sensitive individuals, but that's estimated to be an incidence of about just a little over one in a million doses administered, so it's certainly quite rare. In the past, there were assertions that hepatitis B vaccine could contribute to a number of other illnesses. But I'm happy to say that those hypotheses raised by case reports have been thoroughly tested in well-designed epidemiologic studies, and there is really no substantial evidence that hepatitis B vaccine is contributing to autoimmune phenomenon or to increased risk of other illnesses other than this risk of anaphylaxis in about one in a million doses administered. So, we have very robust data about hepatitis B vaccine safety, and I think the data are very, very

reassuring. In terms of their duration of protection and immunogenicity, because the vaccine has now been in use for over 30 years, both the immunogenicity data and some clinical studies and some modeling studies; all three suggest that not only is the vaccine highly immunogenic, but it probably protects for at least 30 years, if not for life. So, vaccination with any three-dose vaccine series provides seroprotection in about 90% of young adults; 75% of older adults like you and me; and the two-dose schedule with the Heplisav-B® vaccine appears to be equally protective seroprotection levels in those 18-70 years, again in the range of around 90% even in the older age group. So, everything we know about these different vaccines tells us that they're highly immunogenic, very safe, and likely to provide, if not lifetime protection, certainly long-term protection. So, these are among the oldest and best-studied vaccines we have.

DR. SCHAFFNER: For those just tuning in, this is CME on ReachMD. I'm Dr. Bill Schaffner, Medical Director of the National Foundation for Infectious Diseases, and I have the pleasure of speaking with Dr. Arthur Reingold on the topic of preventing hepatitis B in U.S. adults through vaccination. Art, earlier you spoke about the importance for adults at high risk of acquiring HPV to get vaccinated, but as we mentioned earlier, the vaccination rates in the U.S. are still pretty low with only about 25% of adults vaccinated against HPV infection as currently recommended. So, what are some of the barriers to vaccination for these populations?

DR. REINGOLD: I think that's an important question. I think one can divide those barriers into two broad categories; those that relate pretty much to adult vaccination in general, and those that are specific to hepatitis B vaccine. So, among the challenges to vaccinate adults in general, obviously not all adults have unlimited access to healthcare and so access to care is a potential limitation. Secondly, there is generally not high awareness of the need and importance of vaccination of adults, the same way there is for infants, and information about the disease that may prevent, so that's another broad category of limitations. Related to that are incorrect beliefs about vaccine safety and efficacy, which cover many vaccines, and hepatitis B vaccine is no different. Then, in addition, the recommendations for adult vaccination are complicated in many instances, as opposed to vaccinating everybody, they involve subgroups and risk groups and the like. In addition, there are competing priorities during the healthcare visits, in addition to vaccination and often in the adult care setting, there are not reminder and recall systems. And that taken together with the fact that not all healthcare professionals are strongly making these vaccination recommendations to adults, I think those are the broad limitations to adult vaccination. Then in addition, there are some specific issues about hepatitis B vaccine. First of all, again, these are complicated recommendations targeting more than a dozen different groups who would benefit from vaccination, so they're not totally straightforward. Secondly, and perhaps very important, is the fact that two of the leading risk factors for infection of hepatitis B are sexual exposures and injection drug use, and not all patients are comfortable acknowledging those exposures, and perhaps not all healthcare providers are comfortable asking detailed questions about those exposures. In addition, there are, as I understand it, some logistical and financial challenges associated with ordering and stocking hepatitis B vaccine, and then there are some complexities around what the health insurance coverage is for hepatitis B vaccine. So, we have a combination of generic adult vaccination challenges in addition to some that are more specific to this particular vaccine.

DR. SCHAFFNER: That's quite a list of barriers. But there have been addresses to those barriers, so thinking optimistically and proactively, how about leading us through some of those strategies that can address those barriers satisfactorily.

DR. REINGOLD: Sure, I'd be happy to. I think, first of all of course, as I learned in medical school, taking a good history from a patient and trying to ascertain information about their risk behaviors, whether it's smoking or alcohol use or sexual activity or things, certainly should be part of what any good healthcare provider does in taking care of a patient. It's useful to implement standing orders within the clinical setting to try and take some of the opportunity for missing a chance to immunize patients out of the system. There are other ways, of course, to avoid missed vaccination opportunities, but standing orders is certainly a very good one. Developing and implementing processes to track doses and ensure that patients return for follow-up doses can certainly be very, very helpful, and there are certainly healthcare systems that are doing a very good job with respect to processing and tracking doses of vaccines. It is certainly the case that, if it's not already true that hepatitis B vaccinations should be a part of the best practice guidelines for relevant patient populations, the kind of metrics that people measure in order to look at the quality of care, that certainly should be there as an indicator that a practice is doing the best possible job. We can also do a better job of integrating hepatitis B vaccination into nontraditional settings. And I'll come to some of those in a minute, but just to take one example immediately, many of the people who are in correctional facilities and jails and prisons are at risk of hepatitis B infection because of their behaviors outside of prison. Frankly, even within prison there are activities that can lead to hepatitis B virus infection. So, the corrections part of our society offers opportunities to vaccinate incarcerated individuals and a recent Institute of Medicine report on elimination of hepatitis B and C in the United States has a substantial focus how the correctional system can help in that regard. There certainly are other nontraditional settings in which one can offer hepatitis B vaccination, increasing or delivering vaccines in pharmacies and, of course, each state has its own rules, regulations, laws, policies about providing vaccines in nontraditional settings like pharmacies, but that can be an effective strategy. So, I think those are a couple of possibilities. We certainly want to make sure that we're continuing to support disease surveillance at the state and local level and using the data from those surveillance systems to help us target the populations that may be at increased risk. Surveillance is

fundamental to our understanding of the epidemiology of hepatitis B. Another good example of where one can offer hepatitis B vaccine in a somewhat nontraditional setting are in locations that are addressing the needs of injection drug users or people with opioid addictions. Of course, harm reduction and other strategies targeting such individuals represent a delicate balance of what the law says and what public health would like to do in terms of harm reduction but offering hepatitis B vaccine in needle syringe exchange settings and places like that certainly allows one to reach some very high-risk individuals. So in addition, of course, we want to make sure that – and I know time is precious in the medical school curriculum with every minute already spoken for, but we want to make sure the next generation of nurses and doctors are being well educated about the importance of adult vaccination in general, and hepatitis B vaccination in particular, and just going back to the issue of healthcare professionals being vaccinated themselves. Of course, I think we need to lead by example, and we need to make sure that we ourselves are up to date on our vaccination so that if a patient asks, we can say, ‘Well, I’ve had the vaccine and you should too.’ Patients do get a certain amount of comfort from knowing that the healthcare provider not only recommends it, but he or she has received the vaccination themselves.

DR. SCHAFFNER: I couldn’t agree more. And with that whole list of ways to address barriers, I’m actually a bit more optimistic. Thanks. Now, here’s one of the most frequently asked questions that at least I get: Should patients be screened before they’re vaccinated – serologically screened?

DR. REINGOLD: In general, the recommendation is not to screen before administering hepatitis B vaccine. First of all, I want to be clear that everything we know says that, even if you end up giving the vaccine to somebody who is already immune as a result of prior infection or prior vaccination, or you end up giving the vaccine to somebody who is chronically infected with hepatitis B virus, there is no indication that there is any safety concern with regard to that. So, there is really not a problem with regard to administering the vaccine safely without screening. What you fundamentally get into are questions about cost and benefits. And the screening process itself can cost money applied across large numbers of individuals can get to be quite expensive. And of course, it delays administration of the vaccine if you’re going to wait for an antibody result to come back. So, the general recommendations from ACIP and other important advisory groups is not to screen before administering hepatitis B vaccine. Now, screening some individuals, particularly post-vaccination and testing to see if they become immune in response to the regular doses is recommended in some settings, but it is really not recommended for the average patient coming in who we would like to target for vaccination. Now, at the same time, we do want to, as I have already alluded to, screen people for behaviors that might put them at increased risk for hepatitis B virus infection in order to make sure that they take whatever steps they can to reduce transmission to themselves or, if they’re already infected, transmission to others. So just this one example of that, if you are screening and identifying individuals who are chronically infected, we can potentially identify and vaccinate their close contacts, their sexual partners, potentially their household members. So, identifying individuals with chronic infection does have value in terms of guiding prevention efforts. But generally, there is no need to screen people before administering the vaccine.

DR. SCHAFFNER: Art, this is just great. But just before we wrap, do you have any key take-aways for our audience to help prevent HBV infections in U.S. adults?

DR. REINGOLD: Well, not to repeat myself too much, but again I just want to reiterate that, first of all, this is a vaccine in which we have an enormous amount of experience and confidence with regards to its safety, its immunogenicity, and the protection that it offers, so people should be very reassured; healthcare providers and patients, that this is a safe and effective vaccine. But we still have a lot of work to do because only about one in four U.S. adults are vaccinated against hepatitis B as recommended. So, if we’re going to speed up and achieve elimination of hepatitis B in the United States, we don’t want to wait for another 30 or 40 years while we continue to vaccinate infants, we really do want to identify adults who warrant protection and get them vaccinated. In addition, as I’ve already said, beyond the high-risk groups that we’d like to identify and encourage or strongly encourage to be vaccinated, we want to make sure and provide the vaccine to anyone who comes forward and requests it, and we want to become more innovative and proactive in the strategies that we use to achieve higher levels of vaccine coverage. So that’s something that I think both the clinical professions and the public health world need to work on in concert to make sure we’re doing the best possible job of administering this vaccine, whether it’s in the clinic, whether it’s in pharmacies, whether it’s in correctional facilities, or needle syringe exchange programs, we really want to broaden the use of the vaccine and reach as many of the target population as possible.

DR. SCHAFFNER: Well, thanks. With those closing thoughts, I would like to thank my guest, Dr. Arthur Reingold, for speaking to me and our ReachMD audience about hepatitis B. To learn more about preventing hepatitis and other infectious diseases, visit www.nfid.org. Thanks for joining us today, and I’d like to say, if you’re in doubt, vaccinate.

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