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HCV AMONG WOMEN OF CHILDBEARING AGE

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HCV Among Women of Childbearing Age

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Dr. Kushner is an assistant professor in the division of liver diseases at the Icahn School of Medicine at Mount Sinai. She completed her medical school training and internal medicine medicine residency at Mount Sinai fellowship in gastroenterology and Master's in Clinical Epidemiology at the University of Pennsylvania and fellowship in transplant hepatology at the University of California San Francisco for clinical and research interests, focus on clinical predictors, epidemiological trends, and outcomes in viral Hepatitis and in liver disease during pregnancy. But clinical practice encompasses the full spectrum of liver disease from Nash and viral Hepatitis to cirrhosis, and decompensated liver disease. Very pleased to turn it over to you Dr. Kushner.

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Thank you so much, Jeff, and I thank you for the introduction. And thank you for the invitation to speak today. In this pregnancy and opioid use disorder series, and the topic that I'll be discussing today is Hepatitis C among women of childbearing age. These are my disclosures. So today, these are the learning objection objectives of the talk. First, I'll discuss a little bit about the epidemiology of Hepatitis C with a focus on Hepatitis C and individuals of childbearing age and during pregnancy. I'll discuss the currently recommended screening recommendations for Hepatitis C and women of childbearing age and in the context of pregnancy. And finally, I'll discuss current practices in terms of Hepatitis C care and counseling during pregnancy. So when we think about Hepatitis C, and in this population, why is this a population that we should focus on, or specifically address and thinking about Hepatitis C and working towards Hepatitis C elimination, for example. So first is, as we'll see, the epidemiology of Hepatitis C has shifted. And as many of you, of course, already are aware, we're seeing more Hepatitis C in younger individuals, which of course has implications for women, and individuals of childbearing age and during pregnancy. It's also important to consider the impact of Hepatitis C on pregnancy outcomes. So if women are diagnosed with Hepatitis C during pregnancy are known to have Hepatitis C and become pregnant, how do we counsel them about any impacts if there is any, and on pregnancy outcomes? Also, very importantly, we need to think about the risk of perinatal transmission of Hepatitis C, what is the risk of transmission from mother to infant? And can there be anything done to lower this risk or prevent this risk? And folding into that is the recommendations for screening for Hepatitis C? What are the current guidelines for screening for Hepatitis C during pregnancy? And lastly, very interesting and evolving topic is the topic of antiviral therapy. So Hepatitis C treatment, and whether there's a role for treatment of Hepatitis C in the context of pregnancy. So first, a bit about epidemiology. And I'll start with a polling questions. And the question is, in what age group are new Hepatitis C infections, currently most common among women, A is age 15 to 44. B is age 45 to 64, and C is equal across all age groups. Great, so we have a very informed audience today. So 88% answered in age 1544. And

that is correct. And I'll show you some of the studies that have looked at this. So in general, when we look at Hepatitis C in the United States, it's still major public health concern. So 3.5 million estimated cases of chronic Hepatitis C and earlier data, hopefully lower now with all the efforts that we're taking to decrease the Hepatitis C. And among young individuals who inject drugs around 50% are actually women of reproductive age. And as as many are aware, the reason that we're seeing A more Hepatitis C and this younger age group is really related to this epidemic, the opioid epidemic. And this is a study from 2014, which looked at data from 2006 to 2012, in terms of reported incidents of new Hepatitis C infections, and saw a significant increase during this time. And when the people were surveyed the individuals who had Hepatitis C when a portion of them were surveyed three or four of them, or 75% of them had a history of prescription opioid abuse. So clearly, there's a very strong relationship between opioid use and Hepatitis C infections, particularly among young individuals younger than 30 years of age.

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This is a data also looking at this trend, specifically in New York State. And we see that in 2005. When we look at new Hepatitis C infections, predominantly, these infections were seen in the baby boomer age group from around age 40 to 60. And males had a much higher incidence of infection than women. But as you go across the years to 2012, to 2015, and finally 2016, you see a second peak of infection emerging among this younger age group. And females and males have almost equal rates of infections. And of course, that includes reproductive age individuals in this younger age group. This is again, data looking at Hepatitis C specifically and women of childbearing age. And this is looking at national data using the national national notifiable disease surveillance system as well as national quest laboratory data specifically looking at Hepatitis C infections over time among women. And we see that starting around 2012 2013 Hepatitis C infections and ages 15 to 44 surpassed those in age 45 to 64. Which, of course was the answer to the polling question. So we're seeing more Hepatitis C in this younger age group. Also, there's some data to say that among those who are injecting drugs, women may actually be at higher risk of becoming infected with Hepatitis C. This is one interesting study that looked at this, pulling many different studies from around the world. And looking at how common injection drug users became Hepatitis C positive, and actually comparing females to males and found that women were 36% more likely to be Hepatitis C positive than males. And, of course, the question is, why may this be the case? Why May, women who inject drugs be actually at higher risk than men in terms of their risk of Hepatitis C. And I think part of the explanation as has been looked at and some of these studies is that women who inject drugs may have higher incidence of higher injection related risk behaviors, so higher rates of equipment and syringe sharing, more women being more likely than men to be injected by others, more likely than males to have injection drug using sexual partners. And also women may be more likely to face stigma, and as a result be less likely to participate in harm reduction services, placing them at higher risk. In addition, there's also data that women may be less likely to actually complete Hepatitis C treatment once initiated. So I think it's multifactorial, but it is really, when we think about Hepatitis C and how, how connected it is to injection drug use, it really is important to as part of our counseling with Hepatitis C, to also include counseling on harm reduction services and safe injection practices. And I wanted to also draw your attention to

this new guideline that was just recently published last month, which is specifically focused on substance use disorder treatment and pregnant adults. This is one of the New York state guidelines and one of the newer ones published which contains a lot of information about counseling, harm reduction, and approaches to substance use disorder treatment specifically, in pregnant adults. This is the website so I've discussed about the increases in Hepatitis C. In individuals of childbearing age held out specifically during pregnancy have we also seen a change in how commonly we're seeing Hepatitis C, diagnosed during pregnancy or present during pregnancy? So yes, we have and and US Several studies have shown that and this is one of the earlier reports, looking at data from 2009 to 2014. And here they actually used birth certificate data and

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starting around there, there was a provider started indicating on birth certificates whether the mom had Hepatitis C, so they were able to begin to collect this data. And ready from 2009 to 2014. There was a significant increase in Hepatitis C reported from this birth certificate data and 89% increase from 2009 to 2014. In individuals during pregnancy, subsequent studies have also looked at this. So this is another study published a bit later and looked at, again, the birth certificate data as well as laboratory data to look at Hepatitis C being reported during pregnancy as well as among women of childbearing age. And among pregnant women. Hepatitis C testing increased, which is great, but also the positivity rate increased from by about 39%. In this in this report. And this also published more recently, in 2020, again, looked at the National Center for Health Statistics, birth reports and found that Hepatitis C in the context of pregnancy increased by 161%, from 2009 to 2017. So we're seeing an increase in the number of cases during pregnancy. Of course, part of that maybe that providers are more commonly testing for Hepatitis C during pregnancy. But also, of course, reflecting an actual increase in rate of Hepatitis C during pregnancy, which is paralleling the increase we're seeing and individuals of childbearing age. So what are the recommendations for testing for Hepatitis C during pregnancy? Is it routinely done? Is it based on risk? And what are the guidelines currently recommending for testing? So this is another polling question. So what are the current recommendations for Hepatitis C screening during pregnancy? And the choices are a screen all women with risk factors during pregnancy? be screened all one all women during pregnancy? And C screening is not recommended in pregnancy for Hepatitis C? Okay, so again, yes, that the answer that most people chose is correct. The current recommendations are to actually screen all women during pregnancy. But this actually pretty recently became the recommendation and was not the case, even you know, a few years prior. So multiple expert guidelines have weighed in on this issue. And the first one that recommended this in 2018 was the American Association for the Study of liver diseases, a SLD. And the Infectious Disease Society of America, which regularly update their Hepatitis C guidelines. And in 2018, they did make the recommendation that all pregnant women should be tested for Hepatitis C, at the initiation of prenatal care. And it was great that they made this recommendation but really there was has not been very much uptake because of course, the providers that are taking care of women during pregnancy are not necessarily the infectious disease and liver disease specialists but the obstetricians and gynecologist and primary care providers. Subsequent to that, more recently, in March of 2020, a

little over a year ago, the United States Preventive Services Task Force by me also made this recommendation and they updated their recommendation from risk based screening to recommending screening all asymptomatic adults, including pregnant persons for Hepatitis C. And this was really in response to some of those studies that I showed that showed that the prevalence had has significantly increased of Hepatitis C in this population.

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Subsequent to that just fit very soon after the USPS TF the CDC also agreed and just one month later in April of 2020. They also said that Hepatitis C screening is recommended for all pregnant women during each pregnancy, except in settings where the prevalence of Hepatitis C infection is very low is less than point 1%. But still, even after this recommendation, the There was not as much uptake. And a lot of people were saying that, really until the OBGYN society ACOG makes the recommendation that practice really won't change very much. And fortunately, just recently and May of this year, ACOG also finally made the recommendation where previously they had recommended only risk based screening, but now also recommend screening for all pregnant individuals during each pregnancy. So given this update and recommendations, I would anticipate that more and more women will be screened during pregnancy and more diagnoses made in in pregnancy. However, there was a recent survey conducted of providers, prenatal care providers in multiple states in the US and this was published earlier this year. And the survey surveyed prenatal care providers about whether they actually are doing universal screening for Hepatitis C or still are doing risk based screening meaning only screening women who endorse risks such as injection drug use, and others. And in this survey, they found that actually 71% of vast majority of the providers are still only doing risk based screening and not doing universal screening. So I think despite all these expert recommendations, and even from ACOG, the OB GYN society, we still have a long way to go to get up to have uptake of these screening recommendations across different practice settings. There also, it's not just about the providers, whether the providers are remembering to do the screening or recommending the screening, I think we also have to remember that there are patient level barriers as well that may exist, for example, women of certain backgrounds for in this particular study, women of Latina and Asian race, were less likely to receive Hepatitis C screening compared with Caucasian woman. And the reasons may be multifactorial, but they were less likely to actually be screened. In addition, African American women experienced higher burden of sexually transmitted infections in general and may also be less likely to receive quality prenatal care and preventative services. So if there isn't that prenatal care and the initial prenatal visit is missed, then the Hepatitis C screening opportunity may also be missed. So I think, as we work towards Hepatitis C elimination and really try to address Hepatitis C in this population, there are multiple different factors at play, not just provider level factors where they're not recommending screening, but also individual level, community level and system level factors, will need to play a role in improving the uptake of Hepatitis C screening. So in addition to screening for Hepatitis C, during pregnancy, if someone is found to have Hepatitis C during pregnancy, or is known previously to have Hepatitis C, and then they become pregnant, how do we counsel these individuals and how do we monitor them? And are there any specific considerations? So these are recommendations from the liver society guidelines. And generally

speaking, the recommendation is to check the Hepatitis C RNA and liver test at the initiation of prenatal care. And also importantly, assess the risk and discuss with the patient the potential risk of mother to child transmission. Also a recommendation that all pregnant women with Hepatitis C should receive prenatal intrapartum care that is appropriate for their individual obstetric risks.

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Because there is no currently known intervention to reduce Mother Child transmission, and I'll mention a little bit more about that in a few slides. In addition, in pregnant women who are infected with Hepatitis C who develop pruritis, or itching of their skin or jaundice, there should be a high suspicion for intrahepatic cholestasis of pregnancy, which is a complication of pregnancy. I'll mention that a bit later as well. And so there should be the provider should be in tune with that and have a high index of suspicion to work that up if B symptoms are endorsed. And in Hepatitis C infected women with cirrhosis, they should be counseled about the increased risk of maternal adverse maternal and perinatal outcomes that are associated with having advanced liver disease. In addition to To see and tech, the pregnant women should be linked to care so that antiviral treatment can be initiated at the appropriate time. So this is the recommendation, again by the liver infectious disease societies. But again, it's, the recommendation is there but there are multiple challenges to ensure appropriate Linkage to Care. In general, women with Hepatitis C, experienced longer delays from to Hepatitis C treatments. And in my practice, for example, I have definitely struggled with having women come back after pregnancy for postpartum care. And that's a known challenge that that obstetricians face that during pregnancy, the individuals are a captive audience, they have multiple visits to ultrasounds, and everything and after delivery. For the postpartum visit, there's a huge drop off and really challenging to keep keep women engaged in care after after delivery. So I've already mentioned a little bit about this, but as we're speaking about pregnancy outcomes, which pregnancy outcome has not been reported in association with Hepatitis C, so this is another polling question. So which has not been associated and the choices are preterm birth intrahepatic cholestasis of pregnancy, growth restriction, gestational diabetes, or none of the above? Okay, again, yes, that is correct. None of the above is the is the correct choice that the majority chose. And, you know, when we look at studies looking at the impact of Hepatitis C on pregnancy outcomes, there have been a number of large kind of population based studies looking to see whether Hepatitis C has an impact on pregnancy outcomes. And I think when looking at these studies, it's important to realize that there are many confounding factors potentially at play that are hard to tease apart from the actual direct effect of the virus on pregnancy outcomes. For example, for example, if there's coexists in injection drug use that in itself, which may or may not always necessarily be reported during pregnancy, but that in itself can have an impact on pregnancy outcomes. Nonetheless, other studies that have looked at this, there have been associations reported of Hepatitis C with an increased risk of preterm birth, increased risk of growth restriction, and increased risk of low birth weight. And even in this one large Swedish birth registry study of over 2000 women with Hepatitis C, that gave birth, there was even an association with a pretty high relative risk with late neonatal deaths. So adverse outcome in the infants. And

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more recent study from Italy. Also, there was reported association with gestational diabetes as well, mechanism, to me is not entirely clear, but they did see this association. And most notably, I would say, is the association with cholestasis of pregnancy, which is why the guidelines recommend to have a high index of suspicion for color spaces, and women with Hepatitis C, during pregnancy. And this, I think, is the most well established effect associated with Hepatitis C that I do believe, is an direct effect of the virus, as opposed to other confounding factors. And I've also seen this in clinical practice, which does make me believe it that women with Hepatitis C are at significantly increased risk of ColourSpace of pregnancy. And that is important because CO space of pregnancy and turn is associated with adverse fetal outcomes. And so it is something very important to look out for and to counsel women on that if they have Hepatitis C if they do develop those symptoms of itching of the skin, or even that their liver tests begin to rise more than they were at baseline during pregnancy to have a high suspicion to check bile acids, which is the diagnostic tests for close days of pregnancy and then initiate treatment if they do have the condition. And another very important aspect of Hepatitis C during pregnancy is the aspect of perinatal transmission or mother to child transmission. How How common is it? And what can we do to prevent it? And what what do we tell moms about what to expect them? What kind of follow up is needed in their infants and children if they had Hepatitis C during pregnancy? So this is a another polling question. And this question is, what is the approximate rate of perinatal transmission or mother to child transmission of Hepatitis C? So how common is it to see transmission from the mom to the infant during pregnancy? And the choices are 1% 5% 10% 15%, or 20%?

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All right, let's see. Yes. Okay. Again, the majority wins. And the correct choice is close to around 5%. Although the studies really vary in their estimated risk, but generally speaking, that that is probably the closest to what is mostly reported. And this is a study by the author bonobo sure if you see an engraved down there below, but I think this is the the one that I've seen the most cited when, when discussing the risk of transmission. And these are the numbers that I also share with patients that I see if they have Hepatitis C in pregnancy, about the risk and try to explain to them, you know, what, what are the chances that that this may happen? So in this study, this was a review of a systematic review of multiple studies pooled together, and overall, the estimated risk was around 5.8%. However, if the women with Hepatitis C were contracted with HIV, that risk was significantly higher, so around 10.8%. But if you look at the numbers, that estimates and these individual studies, they really are kind of all across the board ranging from 2% to 15%, and HIV negative Hepatitis C infected women, and then and this one, even ranging up to almost 30%. So I think there's still more to learn. But I think for for the moment, these are the numbers that I use in counseling, and I think are the most cited terms of the estimate. So, you know, when you speak to patients about these risks, I think everyone views them differently. But in general, at least in my experience in interacting with pregnant individuals, you know, they the the sentiment that I mostly hear is that they would like to not have any risk, you know, so even though 5.8% Doesn't seem like a very high number, you know, they would like to prevent

this from happening at all, if at all possible. So is there anything that can be done by the option traditions to decrease the risk of transmission from an obstetric management perspective? So one question that sometimes comes up is whether the mode of delivery counts whether delivering the baby through cesarean section versus vaginal delivery makes a difference, and the risk of transmission of Hepatitis C, and there have been multiple studies done to investigate this. And when pulling all the data, there really is no specific, no significant increased risk with either mode of delivery. And so there is no recommendation to recommend one mode of delivery versus the other for the prevention of mother to child transmission. In general, there may be some increased risk when invasive fetal monitoring is done, but the precision of the evidence or the quality of evidence isn't great. That being said, you know, the Society for Maternal Fetal Medicine says that the risks and benefits need to be discussed with the patient because it may increase the risk of transmission. And similarly with prolonged rupture of membranes, that with very prolonged rupture of membranes, there may be an increased risk of transmission, but again, the quality of the evidence is an excellent so I it's hard to make big conclusions from this. And I think in general, the obstetrician does what's best for the for the patient based on obstetric indications. And finally, a question that that patients sometimes bring up is whether Breastfeeding can increase the risk of transmission. And in general, there's no significantly increased risk of transmission through breast milk. But the counseling is that if there's exposure to blood, like with cracked nipples, or then you may say that during that time pump and and defer breastfeeding, but in general, there's no transmission through breast milk.

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And what is the impact if trans Mission occurs, what is the impact on on children. So not surprisingly, mother to child transmission or perinatal transmission is the most common cause of Hepatitis C in children. The good news though, is that many do clear spontaneously. So many infants who are exposed to Hepatitis C, will spontaneously clear by two to three years of age, which is why we don't recommend treatment of the of the infant or child before three years of age. However, in addition to the actual transmission of the virus, that there is some data to suggest that that there may be an impact of having exposure to Hepatitis C, and other aspects, for example, on quality of life, and studies showing that it may have an impact on cognitive function in children, and not to mention impact on caregivers, you know, parental emotional impacts in knowing that there was a transmission of the virus to the infants and child. There's also a higher rates of cirrhosis, not surprisingly, in children who acquire Hepatitis C through at birth because there's more time for the development of cirrhosis and they may develop cirrhosis earlier in life. And then of course, someone who acquired it later. And hepatocellular carcinoma or liver cancer is the most common hepatic malignancy or liver cancer in children. So underlying liver disease is important to of course, recognize in children Hepatitis C is among among that. So what is the current recommendations for testing children who may have been exposed to Hepatitis C, during pregnancy. So these, again, are recommendations from a SLD, which is the liver society. And the recommendation is to have all children born to Hepatitis C, infected women tested with Hepatitis C antibody at or after 18 months of age. The other recommendation is that testing with Hepatitis C RNA or PCR testing can be done earlier. But the optimal timing of such testing is unknown. So these guidelines really strongly recommend to

test the infant at 18 months of age with Hepatitis C antibody, and then after that confirm with confirm that they are positive after age three. Another important recommendation is that the siblings of children with vertically acquired chronic Hepatitis C should be tested for Hepatitis C infection if born from the same mother. And I've actually I do talk discuss that with women that I see with Hepatitis C during pregnancy and make sure to recommend testing of their other children, and have identified one sibling of a infant born who was diagnosed with Hepatitis C at age 11. Because the mother went back and had her other children testing tested. So I think this is a really important part of counseling that we should remember.

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And so even though the recommendation is to test children at 18 months of age, how this is done in practice actually, doesn't happen often. So, you know, this study from the Philadelphia department of health that have over 500 Infants who are born to Hepatitis C positive women, only 16% of them were actually tested. And it's not surprising that this doesn't happen because it you have to wait till 18 months of age to test the infants. And knowing our health system, the communication between specialties often is not does not occur. So for example, the obstetrician does not necessarily have communication with pediatrician, especially if the pediatrician is in another hospital or another practice. And so this may not the the pediatrician may just not be aware of the mother's Hepatitis C status, or the mother may not remember that at 18 months of age that the child needs to be tested. This is another study from Pittsburgh and looked at over 1000 Hepatitis C exposed infants and of those 31% around 1/3 of them actually were enrolled, and that helps us them in wellchild services to were followed by pediatrician, but even among those only 30% were screened for Hepatitis C. So I think this is another aspect of this population that that is really important. Again, when we think about Hepatitis C elimination, because if we are not screening the infants born to mothers with Hepatitis C, we are clearly missing cases. And we need to figure out ways to make this more practical and more doable, so that these cases are not are not missed. So, you know, what is the OBGYN role in ensuring pediatric pediatric testing? I think it's challenging. But of course, ideally, it would be important to somehow communicate with the pediatrician about the maternal Hepatitis C infection, whether there's a best practice alert in the medical record system, or there's some kind of direct communication between the obstetrician and the pediatric provider. You know, that I think we need to think more about how this can be done. But it somehow there needs to be some kind of sign off or communication between the maternal pregnancy provider and the the pediatric provider. And how about treatment in children? So what are the recommendations if there is transmission to the child and their screens, and they're found to be Hepatitis C positive, there is recommendation for treatment of children aged three and over with directly acting antiviral agents. And just recently, in June of this year, the two most common pan genotypic Hepatitis C regimens, so Epclusa, sofosbuvir, velpatasvir, and Maverick glich, Caprivi and pibrentasvir. Both of them, the FDA announced that are they're both approved for treating children aged three and over. So I think, you know, the treatments are available and pediatric formulations starting at age three. So I think this would provide more opportunities to treat the children but of course, again, the first step will be to identify them and to make sure that they're appropriately screened.

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And then finally, what are the treatment recommendations? So what are the the treatment guidelines in women of childbearing age and pregnant women and what is the role for directly acting antiviral agents in in these populations? So from the liver society, the recommendation regarding Hepatitis C treatment and pregnancy. Generally, it says for women of reproductive age with no one Hepatitis C infection, antiviral therapy is recommended before considering pregnancy whenever practical and feasible, to reduce the risk of Hepatitis C transmission to future offspring. So the ideal scenario would be to treat women before they become pregnant women of childbearing age. And now that screening is recommended for all adults aged 18 to 79. If they're if they can be identified before pregnancy, that would be the ideal time to treat and then we don't have to worry about the impact of the Hepatitis C both on the pregnancy outcomes as well as the risk of mother to child transmission. But it's not always possible to identify women of childbearing age or individuals of reproductive age before they become pregnant. And that's partially because otherwise healthy, young individuals of reproductive age might not be even seeing health care providers until they become pregnant, at which point they start following with an obstetrician. So how do we counsel them about treatment if they come to you when they're already pregnant? So from the experts society, it says that despite the lack of a recommendation, treatment can actually be considered during pregnancy on an individual basis after a patient physician discussion about the potential risks and benefits. And this is different than what used to be the recommendation with said, which said that you should not under any circumstance, consider treatment during pregnancy due to unknown risks. But now the guidelines are a little bit more flexible and say that treatment can actually be considered during pregnancy. Furthermore, women who become pregnant while already on Hepatitis C treatment, they should discuss the risks versus benefits of continuing treatment with their providers. So, you know, the guidelines are a little bit wishy washy, they don't really provide specific guidance. However, they are a bit more flexible than what they used to be in saying that treatment during pregnancy is not a complete contraindication and can be considered. So this is more of a an opinion question as health care providers. or, you know, individuals who are working with women with Hepatitis C potentially during pregnancy? Would you consider treating a woman with Hepatitis C during pregnancy? And the state? Yes, no question more of an opinion question. Some may require some thought for this, because it's, I suppose, a little bit controversial still. But let's see what people said. Oh, okay. So 74% said, Yes. Which is great to hear. And I think that this field is definitely evolving. So it's becoming just like experts evolve, it's becoming more acceptable to providers as well. So I think, you know, when we think about antiviral therapy, or directly acting antiviral therapy during pregnancy, there are potential pros and cons. So potential pros, of course, is to cure the mom while she's engaged in pregnancy care. So, again, as I mentioned, oftentimes, otherwise, healthy young individuals are not falling with doctors, but when they're

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being followed during pregnancy care, this would be the time to capture and treat them, there may be a potential beneficial impact of treatment during pregnancy, for example, a decrease in the risk of mother to child transmission, in addition to the question of insurance coverage, so

some individuals lose insurance coverage after pregnancy, so they may only have insurance coverage during pregnancy. And so again, this may be the opportunity to treat them while they have insurance. And of course, it offers the benefit of decreasing community transmission before for example, they become pregnant again, or are injecting drugs and may still be transmitting to others. And also may have a potential decrease on these potentially adverse pregnancy outcomes that are associated with Hepatitis C, for example, like close, they still pregnancy. Another hand there also, there's also the other side, which is that we don't have that much data on safety and pregnancy. Similar to most other medications, there aren't huge databases of the use of these medications, specifically in pregnancy. So human safety data is somewhat limited, as well as safety during breastfeeding. In addition, some would say that, even if there is transmission, there's approved approval for treatment of children as young as they age three. So it's okay if there's transmission, you can treat the child later. And, and, you know, treat the mom after delivery, for example. In addition, you know, we, many of us probably have experiences that sometimes there may be difficulty in accessing these medications in a timely way. And of course, in pregnancy, this would be a very time sensitive period where you would want to treat, you know, during pregnancy, and you may not be able to get the medications in that time sensitive way. And the question of cost effectiveness, for example, whether insurance companies would want to approve treatments specifically during pregnancy and whether it's cost effective as opposed to waiting to treat later. There is some data that has looked at safety even published back in 2015, when we used to have pregnancy categories for safety of medications, looking at some of these earlier, directly acting antiviral regimens. Many of them were considered pregnancy Category B, which many of the medications we use in pregnancy are so they're considered relatively safe. Unfortunately, we actually do now have some published human data from a prospective study. So this is a study that was performed by Dr. Chapel from Pittsburgh and it looked at it was a prospective study, looking at treatment of Hepatitis C during second and third trimesters of pregnancy primarily to establish safety. And the number of mothers recruited was pretty small, only nine, partially because genotype three patients were excluded from the study. So there were some challenges with recruitment. But that being said, all of the ones that completed this study had sustained virologic response and there were really were not significant adverse maternal related adverse events reported. So this is the first now published study of treatment during pregnancy and hopefully will pave the way for more larger studies that can provide additional data on safety and I think we all probably know that it probably will be be very effective as we know that the DBAs are.

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So when we think about all of this in these populations, what are the next steps? And how do we continue to improve the way things are done for these populations, which include individuals of childbearing age, individuals during pregnancy, and of course, infants who are exposed to Hepatitis C during pregnancy. So I think we need dedicated programs for individuals of childbearing age and who are pregnant who are injecting drugs and are living with Hepatitis C so that the care can be co located in one place so that Hepatitis C can be treated, even potentially, during pregnancy, and the same settings where drug use treatment programs are being done. I think we need to now that we have the guidelines for Hepatitis C screening during

pregnancy, the next step is actually make sure making sure that providers are aware of these guidelines and actually are doing Hepatitis C screening during pregnancy so that we can diagnose more individuals and link them to care. The other important issue that that we need to think about is how we can improve the follow up of infants born to mothers with Hepatitis C to make sure that they're not lost. And, you know, found to have cirrhosis years later, but rather diagnosed in a timely way, or screens and diagnosed with Hepatitis C and treated starting at age three. And finally, it'll be important to have larger studies of Hepatitis C treatment in pregnancy to continue to demonstrate safety and efficacy and to make this potential option for individuals during pregnancy. And these are just some conclusions. So again, Hepatitis C in individuals of childbearing age and during pregnancy has really been increasing. And partially, that's because we're screening more and partially because of increased rates due to injection drug use epidemic. And so as a result we really need to focus on on this has an important population to address as we work towards elimination. Reminder that universal screening is now recommended in pregnancy. So you know, for if you work in healthcare settings, it would be helpful to see if it's actually being done. Hepatitis C does increase the risk of pregnancy complications, the one that's most establishes cool stages of pregnancy. So I think that should be an important part of counseling individuals during pregnancy. mother to child transmission rate rates range from six to 11%. Higher and HIV contacted individuals to evaluate for Mother Child transmission infant should be tested at age at 18 months of age. And in terms of treatment in these populations, treatment is recommended in children aged over three, ideally, women or individuals of childbearing age should be treated before pregnancy. But studies are underway for Hepatitis C treatment during pregnancy and and hopefully as we have more data that will become more of a realistic option in clinical practice. So I'll end there. And if anyone has any questions, I'm happy to answer them. And feel free to reach out to me by email, if there any follow up questions.

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Thank you so much, Dr. Kushner, for that comprehensive lecture. You've covered a lot of ground and we already have a few questions coming into the chat, and the q&a. So I'd encourage anyone to please enter your questions. And if you'd like to ask your question directly, we'd love to hear from you, you can raise your hand. And Oksana can unmute you. So don't be shy, feel free to raise your hand as well. So first question is whether obese are able to prescribe Hep C treatment? Or if they have to refer out and you know, I think you said that that's sort of a goal that we should be working towards. So are are there currently, programs out there where Hep C treatment has been integrated into the care for pregnant persons? Are you aware of obese who are doing Hep C treatment or is that something we have to work toward?

49:33

That's a great question. So definitely it will be are able to prescribe and I think, Jeff, you may know more about this, as well. But there are there is some state to state variation in terms of requirements for providers to be able to prescribe Hepatitis C treatment in New York state. Those have been largely eliminated, but maybe in other states. There are some restrictions in terms of unique Got a specialist to prescribe. That being said, I definitely know about least one

OB who is prescribing. And that is Catherine chapel who did that first study of treatment during pregnancy. So she is an obstetrician and she does prescribe antiviral therapy. So, and I would imagine there are others around the country as well. So, you know, I think, I think, at this point, we're still working with the acceptance of the treatment during pregnancy, but I OB is are, there may be some states to see variation, but there I definitely know that there are obese that are prescribing a Hepatitis C treatment.

50:44

Great. Question Can Can HCV learn from the connection obese had to peds during the Zika virus outbreak in 2017? Just off these systems?

50:56

Yeah, that's a great question. I mean, I think, with Zika, you know, part of the identification of issues, quote, unquote, occurred during pregnancy, you know, when when you're doing all of those prenatal ultrasounds, and you see that the infant made infant growth and other features may be affected. And I think in that way, there is that kind of information, of course, is being relayed to the pediatrician. I think the challenge with the Hepatitis C is that, you know, there's really this gap where the pregnant women may be diagnosed with Hepatitis C during pregnancy, but there's not really anything done in terms of monitoring the baby or doing anything different per se, obstetric Glee, and then, you know, all of a sudden that 18 months of age, you have to remember to screen so I think that's part of the challenge that there are no specific findings on you know, prenatal ultrasound or other things that are done during prenatal care, that relate to Hepatitis C, during pregnancy, and so there's that gap in time that makes it more challenging. And I think one thought is the consideration for implementing Hepatitis universal Hepatitis C screening, for example, in the pediatric age group, which current guidelines don't address, although I think the overall the prevalence would be quite low. So it may not be cost effective to do so. But that that is one consideration, I think.

52:29

Thank you. We have a question from our colleague, Nadine, Kyla Murphy at the City Department of Health as to the role of telemedicine, postpartum medical appointments occurring via telemedicine, potentially improving postpartum linkage to Hepatitis C care.

52:46

Yeah, I mean, I think, you know, definitely we've learned from COVID, that telemedicine is quite beneficial, and then can really be helpful in keeping patients engaged. And I think in the OB world, this has been discussed in general with improving postpartum follow up, is there a way that we can, you know, keep individuals more engaged after delivery with telemedicine, I mean, part of the challenge, not surprisingly, is, you know, you have a new baby, you have a lot of competing, you know, challenges, and it's hard to go to an extra appointment, but telemedicine would alleviate that to a degree. And maybe that that would be a way to do it. But I think the other challenge would be somehow maintaining this engagement, you know, up until that time to screen the infant at 18 months. But yes, I think that's a great thought that if we can implement

telemedicine, even during prenatal care, to the degree possible it could help with this linkage and keeping people engaged.

53:55
Thank you this request, to say a bit more about the underlying cause that results in increased rates of cholestasis of pregnancy?

54:06
That's a great question. I've been trying to look into that for a little while. And now, you know, I think if you look at liver disease in general, not just Hepatitis C, there appears to be an increased risk and close stasis of pregnancy, which probably has something to do with that there's underlying liver disease and probably underlying issues with bylaws, the bylaws set processing pathway, which then is further impacting impacted by the high estrogen state in pregnancy. So I think that but I do think that that's kind of a general liver disease explanation. I have not really come across anything that provides a good explanation of why specifically Hepatitis C as opposed to other viral Hepatitis, other liver disease, is that such an increased risk? But that is a really interesting question and And I don't know if anyone knows mechanistically. Why. But that being said, I've definitely seen it in practice to the point where, in fact, I did actually have a patient where I did initiate treatment for Hepatitis C during pregnancy and she had horrible refractory, close days of pregnancy and the only thing that helped her cholestasis was actually eliminating the Hepatitis C it improved amazingly, as the viral load came down. So I do feel that there is a direct impact. I don't fully understand the mechanism of why specifically Hepatitis C though.

55:35
Thank you, Dr. Kushner.

[End Transcript]