Hepatitis C Virus Infection

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Panel's Recommendations
I. Do children with HIV/hepatitis C virus (HCV) coinfection warrant any specific surveillance or monitoring beyond what is recommended for HIV mono-infection and HCV mono-infection? Children with HIV/HCV coinfection should receive the same routine care and monitoring that is recommended for children with HIV mono-infection and children with HCV mono-infection (strong, moderate).
II. Should infants born to birthing parents known to have hepatitis C be tested for HCV infection, and if yes, when and how? Testing for HCV infection should be performed on any infant or child whose birthing parent is known to have hepatitis C (strong, high). As per Centers for Disease Control and Prevention guidelines, all pregnant patients should be tested for hepatitis C with each pregnancy. All children perinatally exposed to HCV should receive a nucleic acid test (NAT) for HCV RNA at age 2–6 months. If not performed earlier, NAT for HCV RNA can be performed at age 7–17 months (strong, high). A negative NAT for HCV RNA at age 2–6 months is highly suggestive (>99% negative predictive value) of no perinatal transmission. Negative anti-HCV immunoglobulin G testing at 18 months is confirmatory of no HCV (strong, low). In consultation with a health care provider with expertise in pediatric hepatitis C management, children who test positive for HCV RNA should have follow-up care through age 3 years to assess eligibility for HCV treatment (strong, high).
III. For infants and children born to birthing parents with HIV/HCV coinfection, do specific obstetric or infant feeding practices reduce the risk of perinatal transmission of HCV? Recommendations on route of delivery and intrapartum management are the same for HIV/HCV coinfection and HIV mono-infection. In the absence of specific data showing safety, people with HIV/HCV coinfection should be advised against breastfeeding (strong, moderate).
IV. For people with HIV/HCV coinfection, does treatment of HCV infection with sustained virologic response prior to pregnancy (as opposed to no treatment or treatment failure) reduce the risk of HCV perinatal transmission? People with HIV/HCV coinfection who are of childbearing potential and wish to become pregnant should be evaluated for treatment of HCV infection prior to conception. They should be treated for HCV infection to reduce their risk of liver disease progression and perinatal transmission of HCV (strong, high). Ribavirin-containing regimens are no longer recommended for treatment of HCV infection given the availability of safer and more efficacious treatment options (strong, high). There are no large-scale clinical trials evaluating the safety of pangenotypic direct-acting antiviral (DAA) regimens during pregnancy. Treatment can be considered on an individual basis after a discussion of the potential risks and benefits (strong, low). See details in the HCV/HIV Coinfection section of the Perinatal Guidelines and the American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) HCV guidance for pregnancy.

V. What counseling should an adolescent with HIV receive to reduce the risk of HCV acquisition/transmission?

All adults and adolescents with HIV should be counseled to avoid injection drug use. If using drugs, they should—

- Avoid reusing and/or sharing needles, *and*
- Be tested for HCV and hepatitis B virus, *and*
- Receive appropriate referral and therapy for substance use disorder (**strong, high**).

Unprotected sex has been linked to HCV transmission, so all adolescents—including those with HIV, multiple sex partners, or sexually transmitted infections—should be advised to use barrier protection (**strong, moderate**).

VI. Among children with HIV/HCV coinfection, which vaccinations to reduce risk of liver disease are available?

Hepatitis A and hepatitis B vaccines are recommended for all children, including those with hepatitis C with or without HIV coinfection, with follow-up serologic confirmation of vaccine response (**strong, low**).

VII. For all children with HCV mono-infection or HIV/HCV coinfection, what are the indications for HCV treatment?

Any child aged 3 years or older with HCV mono-infection or HIV/HCV coinfection should receive treatment with a pangenotypic DAA regimen (**strong, moderate**).

VIII. For all children with hepatitis C, what U.S. Food and Drug Administration (FDA)–approved medications are available for those requiring treatment?

Either of the FDA-approved pangenotypic DAA regimens (sofosbuvir/velpatasvir or glecaprevir/pibrentasvir) can be used for treatment (**strong, high**).

For more information about evaluation for DAA treatment, visit the AASLD/IDSA HCV in Children webpage.

IX. When treating children with HIV/HCV coinfection, are there significant drug–drug interactions between HCV and HIV treatment regimens that require consideration?

Clinically relevant drug–drug interactions have been identified between current FDA-approved pediatric DAA regimens and multiple classes of antiretroviral drugs that may warrant alternate therapy, dose adjustment, or extra monitoring. Reference to current AASLD/IDSA HCV guidance on patients with HIV/HCV coinfection is recommended (**strong, high**).

Rating of Evidence

Strength of Recommendation: Strong; Weak

Quality of Evidence: High; Moderate; Low; Very Low

In this document, the term "breastfeeding" is used to describe feeding a child one's own milk (either direct feeding or with expressed milk). When counseling individuals with HIV about infant feeding, it is important to assess and use their preferred terminology; some transgender men and gender-diverse individuals may prefer using the term "chestfeeding" rather than "breastfeeding." We urge providers to consult community-based resources for more information about inclusive, affirming language around gender in health care settings.

Epidemiology

The prevalence of hepatitis C virus (HCV) infection among children in the U.S. National Health and Nutrition Examination Survey was 0.2% (aged 1–11 years) to 0.4% (aged 12–19 years) in the 1990s[1,2] and fell to less than 0.1% in the subsequent decade.[3] A recent modeling study estimated a prevalence of 0.03% for children aged 0 to 11 years and 0.05% for children aged 12 to 18 years.[4] Centers for Disease Control and Prevention (CDC) modeling predicts that approximately 1,700 new cases of perinatally acquired pediatric HCV infection occur annually.[5] The prevalence of HCV

infection among children with HIV may be significantly higher, with HCV coinfection documented among 1.5% of 535 children with HIV in U.S. pediatric HIV clinical trials in 2003.[6] Higher rates of HCV infection have been documented in some international cohorts of children with HIV, likely due to increased risk of HCV perinatal transmission in pregnant people with poorly controlled HIV infection.[7,8]

Perinatal transmission is the predominant mode of HCV acquisition in infants and younger children.[9,10] Injection drug use is the predominant route of infection in older children; less common modes of transmission include noncommercial body piercing or tattooing, unintentional needle stick injury, household contact or sharing of potentially contaminated personal items, and sexual exposure.[11,12] Before 1992, blood transfusion was a key route of HCV transmission in the United States.

The overall risk for perinatal HCV transmission from a woman with HCV mono-infection ranges from 4% to 10%.[9,13-21] The primary risk factor for perinatal HCV transmission is maternal HCV viremia at delivery, although an absolute threshold for HCV transmission has not been identified.[14,22-27] HCV genotype does not appear to affect the risk of perinatal HCV transmission.[14,20] Although a few studies have suggested that vaginal delivery increases risk of HCV transmission[13,15,17,22] and that HCV can be transmitted during the intrapartum period,[28] most studies have found that mode of delivery does not appear to influence overall perinatal HCV transmission.[10,15,16,18,29-33] In addition, even though HCV RNA can be detected in breast milk, studies of infants born to women with HCV have not demonstrated a higher risk of HCV transmission in breastfed infants than in those who are formula fed.[10,13-16,18,25,28,29,34]

Early studies demonstrated that maternal HIV/HCV coinfection increased the risk of perinatal transmission of HCV, with perinatal HCV transmission rates of 6% to 23% reported for infants born to women with HIV/HCV coinfection.[9,13-15,19,26,30-32,35-40] Furthermore, a few studies suggested that children who have HIV during the perinatal period may be more likely than those who do not have HIV to acquire HCV from mothers with HIV/HCV coinfection.[30,31,37,38] Dual virus transmission was reported in 4% to 10% of children born to mothers with HIV/HCV coinfection.[13,30,35,37,39] HCV RNA levels are hypothesized to be higher among women with HIV/HCV coinfection than in those with HCV mono-infection, which could account, in part, for the increased risk of perinatal HCV transmission from pregnant people with HIV/HCV coinfection. However, not all studies have found higher levels of HCV viremia in mothers with HIV/HCV coinfection.[24,31,36] Several recent studies in the era of routine combination antiretroviral therapy (ART) during pregnancy found that the risk of perinatal HCV transmission is far lower than rates found in historical studies when few or no antiretrovirals (ARVs) were available, suggesting that perinatal transmission of HCV may be significantly reduced in women with HIV who are receiving ART.[40,41]

Recommendations on route of delivery, intrapartum management, and infant feeding are the same for HIV/HCV coinfection and HIV mono-infection. Further details are available in the Perinatal Guidelines and Pediatric Antiretroviral Guidelines.

The incidence of HCV infection in adolescents and young adults has been increasing since 2010. Data from the CDC show an increase in the incidence of acute HCV infection among people aged 20 to 29 years from 0.75 cases per 100,000 population in 2010 to 2.2 cases per 100,000 population in 2022. The incidence rate of acute HCV infection in people aged 20 to 29 years peaked in 2018 at 3.0 cases per 100,000 population, which was the highest at the time but now surpassed by the rate in 30 to 39 year olds of 3.6 cases per 100,000 in 2022.[42] The incidence of HCV infection is higher in

rural areas, and the majority of new infections are in people with a history of injection drug use (IDU).[43-47] HIV is a significant risk factor for HCV acquisition in men who have sex with men (MSM).[46,48] MSM with HIV who were followed in the Multicenter AIDS Cohort Study (MACS) from 1984 to 2011 were almost six times more likely to acquire HCV than MSM who did not have HIV (incident risk ratio 5.98). The incidence rate for HCV infection in MSM with HIV recruited to MACS between 2005 and 2011 was 5.16 per 1,000 person-years.[49] The incidence of HCV infection was somewhat lower in a cohort of MSM with HIV in Boston tested between 2008 and 2009 who had an annualized incidence of 1.63 per 1,000 person-years. Risk factors for HCV acquisition included noninjection drug use and a history of sexually transmitted infections.[50]

Clinical Manifestations

The clinical course of HCV infection appears to be more benign in children with perinatal hepatitis C than in adults with newly acquired hepatitis C.[11,51,52] Most children with hepatitis C are asymptomatic; however, some may experience nonspecific symptoms—such as fatigue, myalgias, and poor weight gain—and develop hepatomegaly.[11,52,53] Intermittent asymptomatic elevations in transaminase levels are common during the first 2 years of life.[53-56] Across studies of children with hepatitis C, 20% to 65% of children had apparent clearance of HCV viremia; 50% had chronic asymptomatic infection, characterized by intermittent viremia, rare hepatomegaly, and usually normal liver transaminase levels; and 30% had chronic active infection with persistent viremia and abnormal transaminase levels.[57,58]

Histopathologic inflammatory changes of chronic hepatitis may be present in children with chronic hepatitis C despite a lack of symptoms, normal serum transaminases, and low HCV RNA levels.[53] Analysis of liver histology in 121 treatment-naive pediatric patients showed some degree of inflammation in all samples, mild fibrosis (Ishak stage 1–2) in 80% of specimens, and cirrhosis in 2% of specimens.[59] Most children with chronic hepatitis C who have undergone liver biopsy and are included in published studies typically have mild-to-moderate liver disease as determined by signs of structural alterations, inflammatory activity, and necrosis.[11,24,52,55] Similar proportions of children with perinatally and parenterally acquired HCV have signs of chronic hepatitis on liver biopsy.[56] A small subset of children may develop severe liver disease. In a study of 60 children with perinatally or transfusion-acquired hepatitis C for a mean duration of 13 years, 12% had significant fibrosis on liver biopsy.[52] Older age at time of infection and elevated serum gamma-glutamyl transpeptidase correlated with fibrosis; serum transaminase levels correlated with inflammation.[52]

In adults with HIV/HCV coinfection, the natural history of HCV infection appears to be accelerated, with more rapid progression to cirrhosis, decompensated liver disease, hepatocellular carcinoma, and death.[60,61] Reports on the effect of ART and immune reconstitution on liver-related mortality in adults with HIV/HCV coinfection are conflicting; some studies show decreases, but others show little difference in liver-related mortality.[62,63] Data are minimal on the effect of HIV/HCV coinfection on the natural history of HCV infection in children and insufficient to draw conclusions about HCV disease progression in children with HIV/HCV coinfection.[9] In a study from Spain in the early ART era comparing children with perinatal HIV/HCV coinfection to those with perinatal HCV mono-infection, HCV viremia and maximum transaminase levels were higher in the children with HIV/HCV coinfection than in those with HCV mono-infection.[64]

Data on the impact of HCV on HIV disease progression in adults are conflicting. Some studies suggest that HCV accelerates HIV progression, but others show no such effect.[9] The effect of pediatric HIV/HCV coinfection on HIV disease progression is also unclear because the number of

children with HIV/HCV coinfection is small and only a few studies have evaluated any potential association. Two studies of children with perinatal HIV/HCV coinfection found no increase in HIV progression. In a study of older children with thalassemia who had HIV or HIV/HCV coinfection through transfusion, disease progression was more rapid and mortality was higher in those with HIV/HCV coinfection than in those with HIV mono-infection.[30,39,65]

Diagnostic Assays

Both serologic assays for anti-HCV antibodies and nucleic acid tests (NATs) for HCV RNA are used to diagnose HCV infection. HCV RNA first becomes detectable 1 to 2 weeks after HCV acquisition, preceding the rather delayed antibody seroconversion that occurs an average of 7 to 8 weeks after acquisition.[66] Third-generation enzyme, chemiluminescent, and microparticle immunoassays for anti-HCV immunoglobulin G have high sensitivities and specificities, though sensitivities are lower in patients with HIV with severe immunosuppression and in acute infection prior to seroconversion. A U.S. Food and Drug Administration (FDA)–approved rapid saliva test is also available for screening adolescents and adults aged 15 years and older.[67,68]

A reactive HCV antibody test can represent current infection or past cleared infection, and the presence of HCV RNA, or HCV viremia, is indicative of current HCV infection. Diagnosis of hepatitis C requires a NAT for HCV RNA, and highly sensitive quantitative real-time polymerase chain reaction (PCR) or transcription-mediated amplification NATs have lower limits of detection of 10 to 15 IU/mL and broad quantitative range.[69]

Treatment

The goal of HCV treatment is to achieve sustained viral response (SVR12; absence of viremia 12 weeks after therapy is complete), which has been shown in adults to reduce the risk of progressive liver fibrosis and hepatocellular carcinoma. Secondary benefits of successful therapy include prevention of transmission of HCV and relief from HCV-related stigma. Because liver disease progresses slowly in most children, no rationale exists currently for urgent treatment of most cases of pediatric HCV. Many children previously included in HCV treatment studies had little or no fibrosis.[70] The relatively few children with more significant fibrosis and/or cirrhosis were often treated.[71]

The current standard of care for adults with hepatitis C is a combination of several direct-acting antivirals (DAAs) that target different HCV proteins. The DAAs are administered orally once a day, leading to rapid and consistent viral clearance, and have a very favorable side effect profile. Two pangenotypic DAA regimens are FDA approved for use in children with hepatitis C who are ages 3 years and older: sofosbuvir/velpatasvir and glecaprevir/pibrentasvir.[72-74] Each of these regimens has weight-based dosing and child-friendly formulations that make administration relatively simple.

Management Recommendations

Do children with HIV/HCV coinfection warrant any specific surveillance or monitoring beyond what is recommended for HIV mono-infection and HCV mono-infection?

Children with HIV/HCV coinfection should receive the same routine care and monitoring that is recommended for children with HIV mono-infection and children with HCV mono-infection ***(strong, moderate).***

Due to conflicting data about the rate of disease progression in children with HIV/HCV coinfection compared to that among children with either HIV mono-infection or HCV mono-infection, no specific additional measures need to be implemented. Surveillance and diagnostic measures recommended for children with HIV/HCV coinfection include those recommended for children with HIV mono-infection and those recommended for children with HCV mono-infection. The involvement of a specialist with experience treating HCV is suggested.

Diagnosis and Testing Recommendations

Making the Diagnosis

Should infants born to pregnant people known to have hepatitis C be tested for HCV, and if yes, when and how?

Testing for HCV should be performed on any child whose birthing parent is known to have hepatitis C ***(strong, high).***

As per CDC guidelines, all pregnant patients should be tested for hepatitis C with each pregnancy.

All children perinatally exposed to HCV should receive a NAT for HCV RNA at age 2 to 6 months. Infants and children aged 7 to 17 months who have not previously been tested should receive a NAT for HCV RNA. Children aged ≥18 months who previously have not been tested should receive an anti-HCV test with reflex to NAT for HCV RNA when anti-HCV is reactive ***(strong, high).***

Undetectable HCV RNA at age 2 to 6 months is highly suggestive (>99% negative predictive value) of perinatal transmission. Perinatally exposed children aged ≥18 months with nonreactive anti-HCV test results do not have hepatitis C ***(strong, low).***

Infants and children with detectable HCV RNA should be managed in consultation with a provider with expertise in pediatric hepatitis C management and receive regular follow-up care until eligible for HCV treatment at age 3 years ***(strong, high).***

Passively transferred maternal HCV antibody can be detected up to age 18 months in infants born to birthing parents with hepatitis C. In a large cohort of children who were HCV exposed but uninfected, anti-HCV antibody was present in 15% of children at 12 months, 5% at 15 months, and 2% at 18 months.[24] Infants who are perinatally exposed to HCV should, therefore, not be tested for anti-HCV before age 18 months. Only the detection of HCV viremia can be used to diagnose HCV infection in at-risk infants aged <18 months.[75]

HCV infection can be diagnosed in infants with perinatal exposure by a NAT to detect HCV RNA after age 1 month. The sensitivity of the HCV RNA testing was low (22%) at birth but increased to 79% at age 1 month and 85% at 6 months in a multisite European study published in 2006.[76] A more recent single-site study utilizing high-sensitivity HCV RNA reverse transcription PCR assays to diagnose perinatal HCV infection at age 2 to 6 months reported a sensitivity of 100% (95% confidence interval, 87.5% to 100%).[77] The use of early NAT at 2 to 6 months is recommended by the CDC to identify infants with hepatitis C, given concerns about loss to follow-up before HCV antibody testing can be done at age ≥18 months.[76]

When testing children age ≥18 months an HCV antibody test when reactive should always be followed automatically by a NAT for HCV RNA. HCV antibody testing without reflex to HCV RNA

when antibody is reactive, is incomplete testing. The detection of HCV RNA confirms current HCV infection, and detected HCV RNA should be managed in consultation with a provider with expertise in pediatric hepatitis C management until eligible for HCV treatment at age 3 years. Children aged 3 years or older should receive HCV treatment.

Prevention Recommendations

Primary Prevention

Preventing Exposure

For infants and children born to birthing parents with HIV/HCV coinfection, do specific obstetric or infant feeding practices reduce the risk of HCV perinatal transmission?

Recommendations on route of delivery and intrapartum management are the same for HIV/HCV coinfection and HIV mono-infection. In the absence of specific data showing safety, people with HIV/HCV coinfection should be advised against breastfeeding ***(strong, moderate).***

No strategy to prevent perinatal HCV transmission has been studied. Elective cesarean delivery is not associated with reduced perinatal transmission of HCV and is not recommended for this purpose for pregnant people with current hepatitis C. Maternal HIV/HCV coinfection does not alter the current recommendation for scheduled cesarean delivery for people with HIV who have HIV RNA levels >1,000 copies/mL near delivery to prevent perinatal HIV transmission.

Observational studies inconsistently associate prolonged duration of ruptured amniotic membranes, internal fetal monitoring, and perineal lacerations/episiotomy with increased risk of HCV transmission.[24,41,78]

Limited data suggest that HCV is not transmitted through breastfeeding and that maternal HCV is not a reason to avoid breastfeeding. However, because of the associated risks of HCV transmission with blood exposure and of HIV transmission with breastfeeding, HIV/HCV coinfected people are advised not to breastfeed. For more information, see the HCV/HIV Coinfection section of the Perinatal Guidelines and the AASLD/IDSA HCV guidance for pregnancy.

For people with HIV/HCV coinfection, does treatment of HCV with sustained virologic response prior to pregnancy (as opposed to no treatment or treatment failure) reduce the risk of HCV perinatal transmission?

People with HIV/HCV coinfection who are of childbearing potential and wish to become pregnant should be evaluated for treatment of HCV ***prior*** *to conception. They should be treated for HCV to reduce their risk of liver disease progression and the risk of perinatal transmission of HCV* ***(strong, high).***

Ribavirin-containing regimens are no longer recommended for treatment of HCV given the availability of safer and more efficacious treatment options ***(strong, high).***

There are no large-scale clinical trials evaluating the safety of pangenotypic DAA regimens in pregnancy. Treatment can be considered on an individual basis after discussion of the potential risks and benefits ***(strong, low).*** *For more information, see the HCV/HIV Coinfection section of the Perinatal Guidelines and the AASLD/IDSA guidance for HCV in pregnancy.*

No clinical trials have specifically assessed the efficacy of the treatment of maternal HCV to prevent future perinatal transmission. However, in observational studies in pregnant women who are anti-HCV reactive, those who lack detectable viremia do not transmit HCV to their children, with only rare exceptions that may relate to low-level or fluctuating maternal viremia. Thus, therapy to eradicate HCV viremia prior to pregnancy is expected to eliminate the risk of perinatal transmission. This option was not previously readily feasible because of the safety concerns for interferon and ribavirin in pregnancy, particularly the teratogenic side effects of ribavirin that preclude its use starting 6 months prior to conception and its potential transfer to infants by a breastfeeding mother.[79] The availability of highly effective interferon- and ribavirin-free combinations of all-oral DAA therapies for HCV infection that are safe in animal models of pregnancy offer a safe option for treating people prior to conception to both cure the infection and prevent future perinatal transmission of HCV.

A small study evaluating the pharmacokinetics of ledipasvir/sofosbuvir in pregnancy demonstrated 100% SVR12 and no safety concerns. Similarly, an international case series of 15 pregnant women treated with ledipasvir/sofosbuvir reported 100% SVR12 and no early safety concerns in the women or their infants.[80,81] Currently, data on the use of pangenotypic regimens during pregnancy are limited, with clinical trials in progress.[82] However, treatment can be considered on an individual basis after a patient–physician discussion about potential risks and benefits.

What counseling should an adolescent with HIV receive to reduce the risk of HCV transmission?

All adults and adolescents with HIV should be counseled to avoid injection drug use. If using drugs, they should—

- Avoid reusing and/or sharing needles,
- Be tested for HCV infection and hepatitis B virus (HBV) infection at a frequency aligned with their ongoing exposure, *and*
- Receive appropriate referral and therapy for substance use disorder **(strong, high).**

Unprotected sex has been linked to HCV transmission, so adolescents with HIV and those with multiple sex partners or sexually transmitted infections should be advised to use barrier protection ***(strong, moderate).***

Other potential exposures to HCV, such as tattooing and body piercing, should also be avoided ***(weak, low).***

No HCV preventative or prophylactic vaccine is available. IDU is the most reported risk factor for HCV infection in the United States. Increased IDU among rural and urban adolescents and young adults has fueled increases of new infections among individuals aged <40 in the United States since 2006, with the highest rates in nonurban communities. This change in epidemiology prompted the current recommendation for one-time screening of all adults 18 years and older and for pregnant people during each pregnancy.[83] Although adolescents were not included in the recommendation, adolescents are among those with IDU and often have been diagnosed with hepatitis C when they are admitted to the hospital after an overdose.[84] Given these circumstances, it is appropriate to adapt HCV screening and testing to younger populations or more frequent intervals based on ongoing risk of HCV exposure.

Multiple outbreaks of HCV infection have been reported among MSM with HIV who do not use injection drugs, linked most strongly with inconsistent condom use and other high-risk practices, including having sex while intoxicated on drugs and having multiple sexual partners. In the era of the message "Undetectable = Untransmittable" or U=U, education about the need to continue to use barrier protection to protect against sexual acquisition of HCV, regardless of HIV status, is important.

Preventing the First Episode of Disease

For children with HIV/HCV coinfection, which vaccinations to reduce risk of liver disease are available?

Hepatitis A and hepatitis B vaccines are recommended for all children, including those with hepatitis C with or without HIV coinfection, with follow-up serologic confirmation of vaccine response ***(strong, low).***

Patients with chronic liver disease, HIV, or both can develop fulminant hepatitis from hepatitis A virus (HAV) or HBV infection.[85] Patients with advanced HCV-related liver disease, HIV, or both may not mount an appropriate immune response to vaccines.[86] Therefore, measurement of HAV and HBV antibody titers 1 to 2 months after completion of the vaccination series is recommended. For more information, see the Hepatitis B Virus section of the Pediatric Opportunistic Infections Guidelines.

Treatment Recommendations

For all children with hepatitis C and children with HIV/HCV coinfection, what are the indications for HCV treatment?

All children aged ≥3 years should receive treatment with an approved pangenotypic DAA regimen regardless of disease severity ***(strong, moderate).***

With prior interferon-based HCV treatment or early versions of DAA regimens, concerns about cost, side effects, and complicated administration prevented these agents from being used for widespread treatment. Currently available pangenotypic DAA regimens can cure virtually all patients with HCV mono-infection and HIV/HCV coinfection; therefore, treatment should be offered to all eligible patients regardless of whether they were previously treated. Evaluation for DAA treatment has been simplified with fewer laboratory tests required prior to initiation.

For more information about evaluation for and monitoring on DAA treatment, visit the AASLD/IDSA HIV guidance on HCV in children.

For all children with hepatitis C, what FDA-approved medications are available for those requiring treatment?

Either of the FDA-approved pangenotypic DAA regimens (sofosbuvir/velpatasvir or glecaprevir/pibrentasvir) can be used for treatment ***(strong, high).***

Two pangenotypic DAA regimens are now approved for use in children as young as 3 years old: sofosbuvir/velpatasvir and glecaprevir/pibrentasvir. Both agents offer similar efficacy in curing HCV

infection, and preference for one versus the other should be based on whichever agent is most easily obtained from public or private insurers for the individual patient.

For more information about dosing by age and weight, visit the AASLD/IDSA HIV guidance on HCV in children.

When treating children with HIV/HCV coinfection, are there significant drug–drug interactions between HCV and HIV treatment regimens that require consideration?

Clinically relevant drug–drug interactions have been identified between current FDA-approved pediatric DAA regimens and multiple classes of ARV drugs that may warrant alternate therapy, dose adjustment, or extra monitoring. Referral to current AASLD/IDSA HCV guidance is recommended ***(strong, high).***

Because treatment of HIV/HCV coinfection includes the challenge of dosing separate multidrug regimens, many studies have examined potential drug interactions. The Patients With HIV/HCV Coinfection section of the AASLD/IDSA HCV Guidance offers a detailed discussion of these potential interactions and should be consulted when considering treatment of any kind. This section includes a summary table to quickly screen for potential drug interactions between HCV DAAs and HIV ARVs. In addition, a summary table on the same webpage offers a quick resource for screening for potential drug interactions.

A few key considerations include the following:

- Velpatasvir can increase concentrations of tenofovir disoproxil fumarate and lead to tenofovir-related renal toxicity. It is unclear at this time whether this is also the case with tenofovir alafenamide. Nevertheless, care should be taken in those patients with reduced creatinine clearance.[87]
- Concentrations of velpatasvir, glecaprevir, and pibrentasvir are significantly reduced when co-administered with efavirenz.[88,89] Thus, both currently approved pediatric pangenotypic DAA regimens (sofosbuvir/velpatasvir and glecaprevir/pibrentasvir) are to be avoided in children taking non-nucleoside reverse transcriptase inhibitors, including efavirenz, etravirine, or nevirapine. No interactions are expected with rilpivirine with either pangenotypic regimen.
- Glecaprevir co-administration is contraindicated with atazanavir and not recommended with ritonavir-boosted ART regimens due to elevated glecepravir concentrations.

Dosing Recommendations and Important Considerations for HCV Antiviral Therapy in Children and Adolescents With HIV

- The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) have developed a web-based process for the rapid formulation and dissemination of evidence-based, expert-developed recommendations for hepatitis C virus (HCV) management. See the AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C for more details.
- For detailed dosing recommendations for HCV antiviral therapy in children and adolescents, refer to the section on HCV in Children.
- For more information on other important considerations in the management of HCV in children and adolescents with HIV—such as drug–drug interactions, alternate therapies, dose adjustment, and extra monitoring—refer to the section on Patients With HIV/HCV Coinfection.

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