**HIV Module: HIV and Hepatitis C**

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Objectives:

* Describe the epidemiology of Hepatitis C (HCV) including HIV co-infection
* Understand screening guidelines and recommendations for HCV
* Describe the clinical manifestations of HCV and usual clinical course if untreated
* Describe the management of HCV infection in patients living with HIV

**Case 1. Mr. Amarillo is a 47 year old man with HIV/AIDS, hypertension, chronic tobacco use and active alcohol use disorder. He has never injected drugs. His HIV is well-controlled on combination antiretroviral therapy. He has sex with men and women but he does not currently have a partner. He shares with you that an old friend of his was recently sick with complications from hepatitis C (HCV), and he wonders if he could be at risk. He recently transferred care to your clinic, and you have no medical records for him. He does not know if he has ever been tested for Hepatitis C. His ROS is negative, specifically for abdominal pain, swelling, or jaundice.**

1. **Describe the epidemiology of HCV in general and in people living with HIV/AIDS.**

Of the approximately 3.5 million people with chronic HCV in the US (2% of the population), half are unaware of their infection. The primary transmission route is exposure to infected blood through injection drug use (IVDU – approximately 60%) or other percutaneous exposure such as health exposures (5%) and blood transfusions before 1992 (10%). Transmission can also occur vertically from mother to child, and through sexual contact (15%), particularly condomless anal sex. It is now the leading infectious cause of death in the US.

People living with HIV are at risk for HCV due to shared transmission routes including IVDU and condomless sex.

1. **Should he be screened for HCV? What are the current guidelines on screening for HCV in patients with HIV/AIDS?**

AllHIV patients should receive one-time HCV testing. In the HIV-negative population, patients should be tested if risk factors are present, including those born 1945-1965 (regardless of risk), with history of IVDU or other occupational or health exposures, tattoos or medical procedures performed in unregulated setting, history of incarceration, or signs/symptoms of liver disease. Sexually active HIV-negative patients starting PrEP should also be screened.

Initial screening is performed with HCV antibody test. If positive, confirmation with HCV-RNA quantification is indicated. HCV RNA test can also be performed if HCV antibody test is negative but liver disease is present, there is strong suspicion for recent infection within 6 months, or the patient is immunocompromised.

If a patient with known prior HCV infection that was successfully treated is re-exposed, repeat testing should be performed with HCV-RNA.

**Case 1, Continued: Mr. Amarillo tests negative for Hepatitis C.**

1. **How would you counsel Mr. Amarillo about his results and future risk for hepatitis C? When and under what conditions should he be tested again in the future?**

After recommended one-time testing (see above), HCV antibody (or RNA) testing can be performed as needed based on risk factors for infection (see below table). Notably, sexual transmission of HCV is rare but possible, especially during anal sex.

| HCV-infected persons should be counseled to avoid sharing toothbrushes and dental or shaving equipment, and be cautioned to cover any bleeding wound to prevent the possibility of others coming into contact with their blood. |
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| Persons should be counseled to stop using illicit drugs and enter substance abuse treatment. Those who continue to inject drugs should be counseled to:* Avoid reusing or sharing syringes, needles, water, cotton, and other drug preparation equipment.
* Use new sterile syringes and filters, and disinfected cookers.
* Clean the injection site with a new alcohol swab.
* Dispose of syringes and needles after 1 use in a safe, puncture-proof container.
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| Persons with HCV infection should be advised not to donate blood and to discuss HCV serostatus prior to donation of body organs, other tissue, or semen. |
| Persons with HIV infection and those with multiple sexual partners or sexually transmitted infections should be encouraged to use barrier precautions to prevent sexual transmission.  |
| Household surfaces and implements contaminated with visible blood from an HCV-infected person should be cleaned using a dilution of 1 part household bleach to 9 parts water. Gloves should be worn when cleaning up blood spills. |

*Adapted from https://www.hcvguidelines.org/evaluate/testing-and-linkage*

**Case 2: Ms. Leber is a 63 year old woman with HTN, CKD stage 3, longstanding HIV/AIDS and a long history of polysubstance use, including injecting heroin. \*\*\* ART regimen She was diagnosed with HCV >10 years ago. She was treated with Interferon and ribavirin in 2010 but had to stop the regimen due to toxicity.**

1. **Describe the natural course of HCV. How does it differ in patients with HIV co-infection?**

Early infection of HCV is typically asymptomatic, however acute infection sometimes presents as symptomatic acute hepatitis with fever, abdominal pain and jaundice. Chronic infection occurs in 75-85% of initially infected patients.

In the long term, hepatic necroinflammation results in fibrosis. Onset and speed of progression of fibrosis is quite variable among individuals. The presence of fibrosis indicates risk for faster progression. Within 30 years, cirrhosis develops in 10-30% of those infected. Once cirrhosis is present, risk of hepatocellular carcinoma (HCC) is increased 20-fold.

Extrahepatic manifestations and associations include mixed cryoglobulinemia, Sjogren’s, thrombocytopenia, porphyria, diabetes mellitus, prurigo nodularis, and membranoproliferative glomerulonephritis.

Chronic alcohol use, particularly >50 g daily, accelerates progression of liver fibrosis and onset of hepatocellular carcinoma (HCC). Factors such as chronic alcohol use, immunosuppression (AIDS, solid organ transplantation, etc), nonalcoholic fatty liver disease (NAFLD), obesity, insulin resisistance, male sex, advanced age, HBV or HIV co-infection, and potentially tobacco use can speed progression of fibrosis. Genotype 3 is also associated with faster progression.

Patients with HIV/HCV co-infection have higher morbidity and mortality and more advanced liver fibrosis and cirrhosis, even in the cART era, than patients with HCV mono-infection. Though treatment of HIV/HCV co-infected patients reduces rates of HCC and decompensated cirrhosis, patients with HIV have historically had low uptake of HCV therapy due to comorbidities, drug interactions and other provider concerns. Early treatment regimens consisted of peginterferon and ribavirin which had cure rates of <50% and were poorly tolerated. With newer DAA regimens result in very high cure rates (> 95%) that are similar in HCV patients with and without HCV.

1. **What testing should be performed when preparing to start a patient on treatment?**

Evaluation of liver disease severity should be evaluated with physical exam, hepatic function panel (AST, ALT, alk phos, albumin, bilirubin), INR, platelet count, creatinine, serum fibrosis marker panels, and imaging. HCV genotype/subtype and viral load should be sent. Patients should be tested for co-occuring infections including HIV and HBV (HBsAg, anti-HBs and anti-HBc).

Since degree of fibrosis is an important prognostic factor, pretreatment assessment shouldinclude evaluation of fibrosis with liver biopsy (gold standard, but invasive) or non-invasive imaging such as ultrasound, CT or transient elastography (FibroScan).

All patients should be treated regardless of baseline fibrosis, in order to prevent morbidity, mortality and ongoing transmission. However, therapy is delayed for many patients, often due to cost. If therapy is to be deferred for any reason, assessment of liver disease should be ongoing, occurring at least yearly (ideal interval not known).

**Case 2, Continued: Ms. Leber’s test results are shown below.**

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INR 1.1

Hepatitis A antibody positive

Anti-HBs and anti-HBc positive, HBsAg negative

Fib-4 = (Age\*AST)/(platelets/√ALT) = 1.4

1. **How would you proceed in managing Ms. Leber’s HCV in the setting of her HIV? What regimens are currently available to treat HCV?**

Ms. Leber’s Fib-4 score is reassuring; a score <1.45 has a negative predictive value of 90% for advanced fibrosis (vs. Fib-4 > 3.25 has 97% specificity for advanced fibrosis and positive predictive value 65%). Therefore, she is unlikely to have significant fibrosis.

Counseling should be performed on abstaining from alcohol and avoiding further exposures to prevent transmission and infection with superinfecting strain.

Vaccination for Hepatitis A and B should be performed.

HIV/HCV-coinfected patients should be managed the same as those without HIV infection (though need to manage interactions with antiretroviral medications – more info available at <https://www.hcvguidelines.org/unique-populations/hiv-hcv> and [www.hep-druginteractions.org](http://www.hep-druginteractions.org/)). New direct acting agents are quickly being approved, and it is best to consult up-to-date guidelines based on the genotype and whether the patient is treatment-naïve or has cirrhosis. Guidelines can be found at <https://www.hcvguidelines.org/treatment-naive>. Current direct acting regimens effective for all genotypes include Epclusa (sofosbuvir/velpatasvir) and Mavyret (glecaprevir/pibrentasvir).

1. **What monitoring should Ms. Leber undergo during and after her treatment?**

During treatment:

* CBC, creatinine, LFTs at 4 weeks, thereafter as needed.
	+ Treatment should be stopped if ALT increases >10x baseline, or <10x baseline but symptomatic (nausea, pain, jaundice)
	+ Asymptomatic low-level ALT elevations should be monitored every 2 weeks.
* Quantitative HCV-RNA should be tested at 4 weeks, and 12 weeks after therapy is completed
	+ If HCV-RNA is detected at week 4, repeat at 6 weeks. If an increase of >10-fold has occurred, stop treatment.

Note: There is Black box warning for HBV reactivation in the setting of HCV treatment with direct-acting antivirals. Therefore, it is very important to test for HBV prior to treatment.

**Resources**

AASLD/IDSA guidelines: “HCV Guidance: Recommendations for Testing, Managing and Treating Hepatitis C”. Available at <https://www.hcvguidelines.org/contents>