

PATIENT ENCOUNTER RESOURCE PACKET FOR PRESCRIBERS EVALUATING PERSONS WITH HEPATITIS C VIRUS (HCV) FOR HCV TREATMENT

While HCV management has historically been a specialty-oriented task in the past, new breakthroughs in the pharmacological treatment of HCV through direct acting antivirals (DAAs) have streamlined the pretreatment assessment, simplified the pharmacological prescribing regimes, dramatically reduced the side effects of treatment, all while increasing the overall cure rates above 98%. In addition to this, Louisiana has launched the Nation's first-of-its-kind HCV elimination plan, Hep C Free LA. This 5-year plan is centered around having unrestricted access to the authorized generic for Epclusa (Sofosbuvir/Velpatasvir) for Medicaid patients and anyone incarcerated in Louisiana.

With the Hep C Free LA plan, the dream of eliminating HCV as a public health threat from Louisiana will only be possible by partnering with primary care providers throughout the state to ensure access to all people in need. This document was created to help provide a road map to assist our partnering prescribers and help support you in our collective fight to end the epidemic.

The following documents serve as a reference guide for any providers looking to offer HCV testing and treatment services in their clinics. This document was designed to give a framework for HCV patient encounters, but each provider has the liberty to practice as they see fit. With COVID-19 driving increased demand for virtual patient encounters and telemedicine, there is a part of this document focusing on transitioning from in person to virtual patient encounters. The Department of Health also maintains a live clinical access warm line at (919) 920-6707 staffed by physicians to provide clinical support for prescribers across the State.

KEY HISTORY ASPECTS FOR PERSONS WITH HEPATITIS C VIRUS (HCV)

- Identify Risk factors for HCV Acquisition
- Alcohol History
- Injection Drug Use History
- Psychiatric History
- Prior Staging of Liver Fibrosis
 - Liver biopsy, it is important to document resulting Fibrosis score
 - Fibrosis staging via alternative method, like Fibrosure or Fibroscan
- Complications of Liver Disease
 - Prior Diagnosis / hospital admissions for:
 - Ascites
 - Hepatic Encephalopathy
 - Jaundice
 - Gastrointestinal bleeding
- HCV-Associated Extrahepatic Manifestations
 - Most common symptoms in patients who had extrahepatic manifestations are: arthralgia, paresthesia, myalgia, pruritus, and sicca syndrome
- Prior HCV Treatment
 - Have they ever been treated?
 - Successful / Unsuccessful
 - Documented Cure / Sustained Virologic Response (SVR12)
 - Type
 - Duration
 - Degree of adherence
 - Adverse effects
- Comorbidities
 - Non-Alcoholic Fatty Liver Disease (NAFLD)
 - Obesity (past or current)
 - Strongly associated with the development of NAFLD.
 - Insulin resistance or Diabetes
 - Dyslipidemia or Hypertriglyceridemia
 - Known history of other liver diseases
- Significant Coinfections
 - Hepatitis A virus (HAV)
 - Hepatitis B virus (HBV)
 - Human immunodeficiency virus (HIV)

KEY PHYSICAL EXAMINATION AND DIAGNOSTIC TESTING ASPECTS FOR PERSONS WITH HEPATITIS C VIRUS (HCV)

KEY ASPECTS OF PHYSICAL EXAMINATION

- Height and weight to determine the body mass index (BMI)
- Clinical signs associated with liver disease:
 - Ascites
 - Lower extremity edema
 - Distended abdominal veins
 - Gynecomastia
 - Scleral icterus
 - Jaundice
 - Palmar erythema
 - Spider nevi (Spider angiomas)/ Telangiectasias
 - Leukonychia, characterized by ground glass opacification of nearly the entire nail, obliteration of the lunula, and a narrow band of normal, pink nail bed at the distal border (Terry's nails)
 - Neuro:
 - Assess alertness, orientation and cognition

KEY ASPECTS OF LABORATORY TESTING

- HCV RNA Viral Load
 - Confirmatory testing for + HCV antibody screening
 - Qualitative or quantitative PCR
- General Labs:
 - Complete blood count (CBC)
 - Complete metabolic profile (CMP)
 - Thyroid function tests (TSH)
- Coinfection Assays:
 - Hepatitis A antibody
 - Hepatitis B surface antigen
 - Hepatitis B core antibody total
 - Hepatitis B surface antibody
 - HIV antibody

KEY ASSESSMENT AND TREATMENT PLAN ASPECTS FOR PERSONS WITH HEPATITIS C VIRUS (HCV)

- Immunizations for Persons Living with HCV (if not immune or up to date)
 - Hepatitis A
 - Hepatitis B
 - Pneumococcal
 - Routine adult vaccines:
 - Yearly influenza
 - Tetanus Diphtheria Acellular Pertussis (Tdap) or Tetanus Diphtheria (Td) booster every 10 years.
- Screening for other causes of liver disease
 - Alcoholic Liver Disease with counseling on alcohol cessation
 - Nonalcoholic Fatty Liver Disease (NAFLD) with counseling on weight loss, strict glycemic and lipid control
- Consideration of starting HCV treatment
 - Need to get initial evaluation of labs back prior to starting treatment
 - Ideally staging should be done before treatment initiation (Fibroscan, FIB-4, APRI, Fibrosure)
 - Decide whether ultrasound needed before starting treatment
 - Recommend ultrasound if liver tests are abnormal
 - Not required before initiated treatment for confirmed HCV
 - Check patient medication list for potential drug / drug interactions
 - Educate patient on HCV, transmission, treatment, risks for progressive liver disease (i.e. EtOH, fatty liver), authorized generic Epclusa treatment details: efficacy, side effects and drug-drug interactions
 - Discuss compliance with medication
 - Outline follow up
 - Link to complimentary services
 - Addiction services if indicated
 - SSP if ongoing risk factors (PWID)
- Follow-up
 - Based on Hep B exposure status and stage of liver fibrosis
 - Check HCV Viral RNA and hepatic function 12 weeks after last dose

CONSIDERATIONS FOR HEPATITIS C VIRUS (HCV) MANAGEMENT IN THE VIRTUAL OFFICE VISIT (TELEMEDICINE)

Virtual office visits are rapidly becoming an integral part of many prescribers' daily work routine. Studies have shown comparable SVR12 (cure) rates in patients who underwent traditional in person office visits and those who were managed via telehealth services. The previous document outlined how to approach any visit with a patient with HCV. This document aims to highlight considerations that might impact the success of a telemedicine encounter. These include patient, provider, clinic, laboratory/radiology factors to think about and address, if needed, to optimize the telemedicine experience and outcome.

PATIENT FACTORS

- Medical literacy and understanding
 - Have a support person also present for the visit so that person can assist with the HCV evaluation and help with HCV treatment understanding and compliance
- Substance use and mental health issues
 - Fully explore patient's substance use and mental health issues to assess how they may impact HCV treatment, and inform your decision to start treatment via telemedicine
- Medical complexity and stability
 - Fully explore any ongoing medical issues or evaluations that may interfere with completing the HCV evaluation or treatment
- Assessment of patient compliance
 - Take into consideration the issues mentioned above along with your impression during the telemedicine visit and determine if patient compliance may interfere HCV evaluation and treatment
- New versus established patient
 - Since providers are usually more familiar with established patients it may be easier to start HCV treatment on the telemedicine visit if the patient has already been established. For a new patient, the provider may need more time to understand and explore the above considerations and prefer waiting to prescribe HCV treatment until a follow-up appointment. Although the evaluation for HCV (i.e. labs and staging) can be ordered at the first telemedicine visit
 - HCV treatment can be started at or soon after the first telemedicine visit based on provider comfort

PROVIDER FACTORS

- Provider comfort and confidence with HCV evaluation and treatment
 - The more comfortable and/or experienced a provider is with HCV evaluation and treatment it will likely be easier to initiate therapy via telemedicine

CLINICAL FACTORS

- Clinic plans for in person visits
 - Assess readiness for clinic to see patients in person vs via telemedicine to maximize safety and minimize wait times.
- Quick and clear communication between the provider and the clinic staff, and then the clinic staff and the patient
 - One the same day of the appointment the provider should make it clear to the clinic staff what the patient needs done. The clinic staff on the same day should follow up with the patient regarding the plan, any upcoming lab/radiology appointments, and follow-up appointment (either telemedicine or in person)

LABORATORY AND RADIOLOGY FACTORS

- Understand patient's access to laboratory and radiology services
 - Need to make sure patients can get the needed labs to undergo HCV evaluation and start treatment. Providers and patients need to understand the impact in time delays for getting those labs and staging complete. With certain populations in person visits may be needed to facilitate needed lab work
 - Need to make it clear to patients that certain labs and radiology are required to better understand their degree of liver disease from HCV and to start HCV treatment

WHEN TELEMEDICINE MAY NOT BE APPROPRIATE

- Decompensated liver disease (bleeding, ascites, encephalopathy, jaundice)
- Consideration of referral for a liver transplant
- Emergent or urgent medical/psychiatric conditions

EPIC TEMPLATE PRIMARY CARE HEPATITIS C VIRUS CLINICAL NOTE

Subjective:

@NAME@ is here for HCV.

HPI

@NAME@ has been feeling

Possible risk factor for HCV:

Possible time of exposure:

Previous heavy EtOH:

Current EtOH:

Previous drug use:

Psychiatric issues

Current drug use:

Previous HCV treatment:

No evidence of ascites, jaundice, confusion or gastrointestinal bleeding.

@ROSCV@

Objective:

@PHYEXAMBYAGE@

@RESUFAST(WBC,HGB,HCT,PLT,ALT,AST,NA,K,CL,CREATININE,BUN,CO2,INR,G
LUF)@

@RESUFAST(LABPROT,LABALBU)@

HCV staging (Fibroscan, APRI, FIB-4, Fibrosure):

Abdominal imaging:

Hep A and B immune status:

Hep A IgG

HepBs Ab

HIV status:

HIV Ab

Hep Bs Ag status:

HepBsAg

HepBc IgG total

EPIC TEMPLATE PRIMARY CARE HEPATITIS C VIRUS CLINICAL NOTE (CONT)

Assessment/Plan:

@DIAGX@

@NAME@ is a @AGE@ @SEX@ with chronic HCV infection. Patient would benefit from treatment.

HCV

- Educated patient on HCV and risk factors for transmission
- Educated about importance of HCV staging/fibrosis determination
- Will proceed with HCV treatment, generic Epclusa for 12 weeks
- Patient was counseled on the importance of medication compliance for the full 12 weeks; advised to contact me if 7 days missed
- Educated patient on most common side effects (headache, fatigue, insomnia, nausea, diarrhea)
- Educated patient while on medication to avoid acid suppressing medications or notify MD if they are needed
- Basic drug interactions reviewed (PPIs, statins, cardiac, seizure meds) and the med changes are as follows:
- Needs hepatic function at 4 weeks on treatment if isolated HBcAb IgG+; otherwise no monitoring needed on treatment
- Check hepatic function and HCV viral load 12 weeks after treatment complete
- Counseled patient on risk of heavy drinking
- Advised against alcohol use while on treatment
- Based on staging will decide if long term follow up is needed; if needed will refer to hepatology clinic
- If cirrhotic will get US and AFP every 6 months until patient can be seen by specialist
- Will vaccinate for hep A and B as needed

RTC in 6 months, around 12 weeks post-treatment

References

1. Guss D, Sherigar J, Rosen P, Mohanty SR. Diagnosis and Management of Hepatitis C Infection in Primary Care Settings. *J Gen Intern Med.* 2018;33:551-7.
[\[PubMed Abstract\]](#)
2. Arora S, Thornton K, Murata G, et al. Outcomes of treatment for hepatitis C virus infection by primary care providers. *N Engl J Med.* 2011;364:2199-207.
[\[PubMed Abstract\]](#)
3. Arora S, Thornton K, Jenkusky SM, Parish B, Scaletti JV. Project ECHO: linking university specialists with rural and prison-based clinicians to improve care for people with chronic hepatitis C in New Mexico. *Public Health Rep.* 2007;122 Suppl 2:74-7.
[\[PubMed Abstract\]](#)
4. Centers for Disease Control and Prevention (CDC). Testing for HCV infection: an update of guidance for clinicians and laboratorians. *MMWR Morb Mortal Wkly Rep.* 2013;62:362-5.
[\[PubMed Abstract\]](#)
5. Bräu N. Evaluation of the hepatitis C virus-infected patient: the initial encounter. *Clin Infect Dis.* 2013;56:853-60.
[\[PubMed Abstract\]](#)
6. Bialek SR, Terrault NA. The changing epidemiology and natural history of hepatitis C virus infection. *Clin Liver Dis.* 2006;10:697-715.
[\[PubMed Abstract\]](#)
7. Zibbell JE, Asher AK, Patel RC, et al. Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014. *Am J Public Health.* 2018;108:175-181.
[\[PubMed Abstract\]](#)
8. Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep.* 2015;64:453-8.
[\[PubMed Abstract\]](#)
9. Charre C, Cotte L, Kramer R, et al. Hepatitis C virus spread from HIV-positive to HIV-negative men who have sex with men. *PLoS One.* 2018;13:e0190340.
[\[PubMed Abstract\]](#)
10. van de Laar TJ, Matthews GV, Prins M, Danta M. Acute hepatitis C in HIV-infected men who have sex with men: an emerging sexually transmitted infection. *AIDS.* 2010;24:1799-812
[\[PubMed Abstract\]](#)
11. Hagan H, Neurer J, Jordan AE, et al. Hepatitis C virus infection among HIV-positive men who have sex with men: protocol for a systematic review and meta-analysis. *Syst Rev.* 2014;3:31.
[\[PubMed Abstract\]](#)
12. Bradshaw D1, Matthews G, Danta M. Sexually transmitted hepatitis C infection: the new epidemic in MSM? *Curr Opin Infect Dis.* 2013;26:66-72.
[\[PubMed Abstract\]](#)
13. Chen CM, Yoon YH, Yi HY, Lucas DL. Alcohol and hepatitis C mortality among males and females in the United States: a life table analysis. *Alcohol Clin Exp Res.* 2007;31:285-92.
[\[PubMed Abstract\]](#)
14. Poynard T, Ratziu V, Charlotte F, Goodman Z, McHutchison J, Albrecht J. Rates and risk factors of liver fibrosis progression in patients with chronic hepatitis C. *J Hepatol.* 2001;34:730-9.
[\[PubMed Abstract\]](#)
15. Bradley KA, Bush KR, Epler AJ, et al. Two brief alcohol-screening tests from the Alcohol Use Disorders Identification Test (AUDIT): validation in a female Veterans Affairs patient population. *Arch Intern Med.* 2003;163:821-9.
[\[PubMed Abstract\]](#)
16. Buchsbaum DG, Buchanan RG, Centor RM, Schnoll SH, Lawton MJ. Screening for alcohol abuse using CAGE scores and likelihood ratios. *Ann Intern Med.* 1991;115:774-7.
[\[PubMed Abstract\]](#)
17. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA.* 1984;252:1905-7.
[\[PubMed Abstract\]](#)
18. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. *Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test.* *Arch Intern Med.* 1998;158:1789-95.
[\[PubMed Abstract\]](#)
19. Cox AL, Thomas DL. Hepatitis C virus vaccines among people who inject drugs. *Clin Infect Dis.* 2013;57 Suppl 2:S46-50.
[\[PubMed Abstract\]](#)
20. Fill MA, Sizemore LA, Rickles M, et al. Epidemiology and risk factors for hepatitis C virus infection in a high-prevalence population. *Epidemiol Infect.* 2018;1-7.
[\[PubMed Abstract\]](#)

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21. Page K, Morris MD, Hahn JA, Maher L, Prins M. Injection drug use and hepatitis C virus infection in young adult injectors: using evidence to inform comprehensive prevention. *Clin Infect Dis*. 2013;57 Suppl 2:S32-8.
[PubMed Abstract]
22. AASLD-IDSAs. Recommendations for testing, management, and treating hepatitis C. When and in whom to initiate HCV therapy.
[AASLD-IDSAs Hepatitis C Guidance]
23. Falade-Nwulia O, Sulkowski MS, Merkow A, Latkin C, Mehta SH. Understanding and addressing hepatitis C reinfection in the oral direct-acting antiviral era. *J Viral Hepat*. 2018;25:220-227.
[PubMed Abstract]
24. Grady BP, Schinkel J, Thomas XV, Dalgard O. Hepatitis C virus reinfection following treatment among people who use drugs. *Clin Infect Dis*. 2013;57 Suppl 2:S105-10.
[PubMed Abstract]
25. Martinello M, Hajarizadeh B, Grebely J, Dore GJ, Matthews GV. HCV Cure and Reinfection Among People With HIV/HCV Coinfection and People Who Inject Drugs. *Curr HIV/AIDS Rep*. 2017;14:110-121.
[PubMed Abstract]
26. Castera L. Noninvasive methods to assess liver disease in patients with hepatitis B or C. *Gastroenterology*. 2012;142:1293-1302.e4.
[PubMed Abstract]
27. Theise ND. Liver biopsy assessment in chronic viral hepatitis: a personal, practical approach. *Mod Pathol*. 2007;20 Suppl 1:S3-14.
[PubMed Abstract]
28. Sherman AC, Sherman KE. Extrahepatic manifestations of hepatitis C infection: navigating CHASM. *Curr HIV/AIDS Rep*. 2015;12:353-61.
[PubMed Abstract]
29. Younossi Z, Park H, Henry L, Adeyemi A, Stepanova M. Extrahepatic Manifestations of Hepatitis C: A Meta-analysis of Prevalence, Quality of Life, and Economic Burden. *Gastroenterology*. 2016;150:1599-1608.
[PubMed Abstract]
30. Cacoub P, Poynard T, Ghillani P, et al. Extrahepatic manifestations of chronic hepatitis C. MULTIVIRC Group. *Multidepartment Virus C. Arthritis Rheum*. 1999;42:2204-12.
[PubMed Abstract]
31. AASLD-IDSAs. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy failed.
[AASLD-IDSAs Hepatitis C Guidance]
32. Czaja AJ. Review article: next-generation transformative advances in the pathogenesis and management of autoimmune hepatitis. *Aliment Pharmacol Ther*. 2017;46:920-937.
[PubMed Abstract]
33. Pascale A, Pais R, Ratziu V. An overview of nonalcoholic steatohepatitis: past, present and future directions. *J Gastrointest Liver Dis*. 2010;19:415-23.
[PubMed Abstract]
34. Krawitt EL. Autoimmune hepatitis. *N Engl J Med*. 2006;354:54-66.
[PubMed Abstract]
35. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. *Gastroenterology*. 2012;142:1592-609.
[PubMed Abstract]
36. Pappachan JM, Babu S, Krishnan B, Ravindran NC. Non-alcoholic Fatty Liver Disease: A Clinical Update. *J Clin Transl Hepatol*. 2017;5:384-393.
[PubMed Abstract]
37. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS; American Association for the Study of Liver Diseases. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. *Hepatology*. 2011;54:328-43.
[PubMed Abstract]
38. Nelson DR, Teckman J, Di Bisceglie AM, Brenner DA. Diagnosis and management of patients with α 1-antitrypsin (A1AT) deficiency. *Clin Gastroenterol Hepatol*. 2012;10:575-80.
[PubMed Abstract]
39. Diehl AM, Day C. Cause, Pathogenesis, and Treatment of Nonalcoholic Steatohepatitis. *N Engl J Med*. 2017;377:2063-2072.
[PubMed Abstract]
40. Vento S, Garofano T, Renzini C, et al. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. *N Engl J Med*. 1998;338:286-90.
[PubMed Abstract]
41. Jamma S, Hussain G, Lau DT. Current Concepts of HBV/HCV Coinfection: Coexistence, but Not Necessarily in Harmony. *Curr Hepat Rep*. 2010;9:260-9.
[PubMed Abstract]

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Last Updated: September 25th, 2020

42. Kim AY, Onofrey S, Church DR. An epidemiologic update on hepatitis C infection in persons living with or at risk of HIV infection. *J Infect Dis.* 2013;207 Suppl 1:S1-6.
[[PubMed Abstract](#)]
43. Chasser Y, Kim AY, Freudenreich O. Hepatitis C Treatment: Clinical Issues for Psychiatrists in the Post-Interferon Era. *Psychosomatics.* 2017;58:1-10.
[[PubMed Abstract](#)]
44. Hauser P, Kern S. Psychiatric and substance use disorders co-morbidities and hepatitis C: Diagnostic and treatment implications. *World J Hepatol.* 2015;7:1921-35.
[[PubMed Abstract](#)]
45. Rifai MA, Indest D, Loftis J, Hauser P. Psychiatric management of the hepatitis C patient. *Curr Treat Options Gastroenterol.* 2006;9:508-19.
[[PubMed Abstract](#)]
46. McGowan CE, Fried MW. Barriers to hepatitis C treatment. *Liver Int.* 2012;32 Suppl 1:151-6.
[[PubMed Abstract](#)]
47. Sockalingam S, Tseng A, Giguere P, Wong D. Psychiatric treatment considerations with direct acting antivirals in hepatitis C. *BMC Gastroenterol.* 2013;13:86.
[[PubMed Abstract](#)]
48. de Bruyn G, Graviss EA. A systematic review of the diagnostic accuracy of physical examination for the detection of cirrhosis. *BMC Med Inform Decis Mak.* 2001;1:6.
[[PubMed Abstract](#)]
49. Udell JA, Wang CS, Tinmouth J, et al. Does this patient with liver disease have cirrhosis? *JAMA.* 2012;307:832-42.
[[PubMed Abstract](#)]
50. Satapathy SK, Bernstein D. Dermatologic disorders and the liver. *Clin Liver Dis.* 2011;15:165-82.
[[PubMed Abstract](#)]
51. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. *Am Fam Physician.* 2006;74:756-62.
[[PubMed Abstract](#)]
52. Cattau EL Jr, Benjamin SB, Knuff TE, Castell DO. The accuracy of the physical examination in the diagnosis of suspected ascites. *JAMA.* 1982;247:1164-6.
[[PubMed Abstract](#)]
53. Kim Sh, Keum B, Kim E, Jeon Y, Chun H. Hepatobiliary and pancreatic: Caput medusae. *J Gastroenterol Hepatol.* 2014;29:1952.
[[PubMed Abstract](#)]
54. Yang PM, Chen DS. Images in clinical medicine. Caput medusae. *N Engl J Med.* 2005;353:e19.
[[PubMed Abstract](#)]
55. Braunstein GD. Clinical practice. Gynecomastia. *N Engl J Med.* 2007;357:1229-37.
[[PubMed Abstract](#)]
56. Dickson G. Gynecomastia. *Am Fam Physician.* 2012;85:716-22.
[[PubMed Abstract](#)]
57. Ruiz MA, Saab S, Rickman LS. The clinical detection of scleral icterus: observations of multiple examiners. *Mil Med.* 1997;162:560-3.
[[PubMed Abstract](#)]
58. Serrao R, Zirwas M, English JC. Palmar erythema. *Am J Clin Dermatol.* 2007;8:347-56.
[[PubMed Abstract](#)]
59. Khasnis A, Gokula RM. Spider nevus. *J Postgrad Med.* 2002;48:307-9.
[[PubMed Abstract](#)]
60. Li CP, Lee FY, Hwang SJ, et al. Spider angiomas in patients with liver cirrhosis: role of vascular endothelial growth factor and basic fibroblast growth factor. *World J Gastroenterol.* 2003;9:2832-5.
[[PubMed Abstract](#)]
61. Pitukweerakul S, Pilla S. Terry's Nails and Lindsay's Nails: Two Nail Abnormalities in Chronic Systemic Diseases. *J Gen Intern Med.* 2016;31:970.
[[PubMed Abstract](#)]
62. Holzberg M, Walker HK. Terry's nails: revised definition and new correlations. *Lancet.* 1984;1:896-9.
[[PubMed Abstract](#)]
63. Advisory Committee on Immunization Practices (ACIP), Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55:1-23.
[[PubMed Abstract](#)]
64. Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep.* 2006;55:1-33; quiz CE1-4.
[[PubMed Abstract](#)]
65. A Two-Dose Hepatitis B Vaccine for Adults (Heplisav-B). *JAMA.* 2018;319:822-823.
[[PubMed Abstract](#)]

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Last Updated: September 25th, 2020

66. Jackson S, Lentino J, Kopp J, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. *Vaccine*. 2018;36:668-674.
[PubMed Abstract]
67. Advisory Committee on Immunization Practices. Recommended Immunization Schedule for Adults Aged 19 Years or Older by Medical Conditions and Other Indications, United States, 2018
[ACIP]
68. Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices. Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). *MMWR Morb Mortal Wkly Rep*. 2010;59:1102-6.
[PubMed Abstract]
69. Batts KP. Iron overload syndromes and the liver. *Mod Pathol*. 2007;20 Suppl 1:S31-9.
[PubMed Abstract]
70. Singal AK, Bataller R, Ahn J, Kamath PS, Shah VH. ACG Clinical Guideline: Alcoholic Liver Disease. *Am J Gastroenterol*. 2018;113:175-194.
[PubMed Abstract]
71. Tome S, Lucey MR. Review article: current management of alcoholic liver disease. *Aliment Pharmacol Ther*. 2004;19:707-14.
[PubMed Abstract]
72. Cohen JA, Kaplan MM. The SGOT/SGPT ratio--an indicator of alcoholic liver disease. *Dig Dis Sci*. 1979;24:835-8.
[PubMed Abstract]
73. Lucey MR, Mathurin P, Morgan TR. Alcoholic hepatitis. *N Engl J Med*. 2009;360:2758-69.
[PubMed Abstract]
74. Dugum M, McCullough A. Diagnosis and Management of Alcoholic Liver Disease. *J Clin Transl Hepatol*. 2015;3:109-16.
[PubMed Abstract]
75. Wiley TE, McCarthy M, Breidi L, McCarthy M, Layden TJ. Impact of alcohol on the histological and clinical progression of hepatitis C infection. *Hepatology*. 1998;28:805-9.
[PubMed Abstract]
76. Poynard T, Bedossa P, Opolon P. *Lancet*. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. *Lancet*. 1997;349:825-32.
[PubMed Abstract]
77. AASLD-IDSAs. Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.
[AASLD-IDSAs Hepatitis C Guidance]
78. Younossi Z, Anstee QM, Marietti M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol*. 2018;15:11-20.
[PubMed Abstract]
79. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;64:73-84.
[PubMed Abstract]
80. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67:328-357.
[AASLD]
81. Diehl AM, Day C. Cause, Pathogenesis, and Treatment of Nonalcoholic Steatohepatitis. *N Engl J Med*. 2017;377:2063-2072.
[PubMed Abstract]
82. Marciniak SJ, Lomas DA. Alpha1-antitrypsin deficiency and autophagy. *N Engl J Med*. 2010;363:1863-4.
[PubMed Abstract]
83. Stoller JK, Aboussouan LS. Alpha1-antitrypsin deficiency. *Lancet*. 2005;365:2225-36.
[PubMed Abstract]
84. Brandhagen DJ, Fairbanks VF, Baldus W. Recognition and management of hereditary hemochromatosis. *Am Fam Physician*. 2002;65:853-60.
[PubMed Abstract]
85. Fleming RE, Ponka P. Iron overload in human disease. *N Engl J Med*. 2012;366:348-59.
[PubMed Abstract]
86. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. *Hepatology*. 2011;54:328-43.
[PubMed Abstract]
87. Qaseem A, Aronson M, Fitterman N, Snow V, Weiss KB, Owens DK. Screening for hereditary hemochromatosis: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2005;143:517-21.
[PubMed Abstract]

FOR REFERENCE PURPOSES ONLY: It is the prescriber's responsibility to remain up to date with the latest guidelines and recommendations regarding hepatitis, screening for hepatitides, treatment recommendations, and prescriber information for any medications used. Questions or concerns from providers can be directed to the HCV Prescriber Warm Line for any clinical questions that may arise.
Last Updated: September 25th, 2020

88. Schmitt B, Golub RM, Green R. Screening primary care patients for hereditary hemochromatosis with transferrin saturation and serum ferritin level: systematic review for the American College of Physicians. *Ann Intern Med.* 2005;143:522-36. [\[PubMed Abstract\]](#)
89. Manns MP, Lohse AW, Vergani D. Autoimmune hepatitis--Update 2015. *J Hepatol.* 2015;62:S100-11. [\[PubMed Abstract\]](#)
90. Mieli-Vergani G, Vergani D, Czaja AJ, et al. Autoimmune hepatitis. *Nat Rev Dis Primers.* 2018;4:18017. [\[PubMed Abstract\]](#)
91. Manns MP, Czaja AJ, Gorham JD, et al. Diagnosis and management of autoimmune hepatitis. *Hepatology.* 2010;51:2193-213. [\[PubMed Abstract\]](#)
92. Czaja AJ, Freese DK; American Association for the Study of Liver Disease. Diagnosis and treatment of autoimmune hepatitis. *Hepatology.* 2002;36:479-97. [\[PubMed Abstract\]](#)
93. Hennes EM, Zeniya M, Czaja AJ, et al. Simplified criteria for the diagnosis of autoimmune hepatitis. *Hepatology.* 2008;48:169-76. [\[PubMed Abstract\]](#)
94. Ahmed A, Wong RJ, Harrison SA. Nonalcoholic Fatty Liver Disease Review: Diagnosis, Treatment, and Outcomes. *Clin Gastroenterol Hepatol.* 2015;13:2062-70. [\[PubMed Abstract\]](#)
95. Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med.* 1999;341:556-62. [\[PubMed Abstract\]](#)
96. Alter MJ. Hepatitis C virus infection in the United States. *J Hepatol.* 1999;31 Suppl 1:88-91. [\[PubMed Abstract\]](#)
97. Karnath B. Stigmata of chronic liver disease. *Hospital Physician.* 2003;39:14-16. [\[Turner White Communications, Inc.\]](#)
98. Li CP, Lee FY, Hwang SJ, et al. Role of substance P in the pathogenesis of spider angiomas in patients with nonalcoholic liver cirrhosis. *Am J Gastroenterol.* 1999;94:502-7. [\[PubMed Abstract\]](#)
99. Missiha SB, Ostrowski M, Heathcote EJ. Disease progression in chronic hepatitis C: modifiable and nonmodifiable factors. *Gastroenterology.* 2008;134:1699-714. [\[PubMed Abstract\]](#)
100. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. *JAMA.* 2015;313:2263-73. [\[PubMed Abstract\]](#)
101. Stevenson M, Lloyd-Jones M, Morgan MY, Wong R. Non-invasive diagnostic assessment tools for the detection of liver fibrosis in patients with suspected alcohol-related liver disease: a systematic review and economic evaluation. *Health Technol Assess.* 2012;16:1-174. [\[PubMed Abstract\]](#)
102. Thomas DL, Thio CL, Martin MP, et al. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. *Nature.* 2009;461:798-801. [\[PubMed Abstract\]](#)
103. Yasui S, Fujiwara K, Yokosuka O. Autoimmune fulminant hepatic failure in chronic hepatitis C during Peg-interferon-alpha 2b plus ribavirin treatment showing histological heterogeneity. *Dig Liver Dis.* 2011;43:666-7. [\[PubMed Abstract\]](#)
104. Yee LJ, Weiss HL, Langner RG, Herrera J, Kaslow RA, van Leeuwen DJ. Risk factors for acquisition of hepatitis C virus infection: a case series and potential implications for disease surveillance. *BMC Infect Dis.* 2001;1:8. [\[PubMed Abstract\]](#)