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Chronic HCV Infection:

A Guide to Pretreatment Laboratory and Other Assessments

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What Pretreatment Assessments Should Be Considered After Chronic HCV Diagnosis?

Laboratory workup is recommended before a treatment is chosen.[1] Pretreatment assessments can help to identify a patient's fibrosis/cirrhosis status, and determine which patients are eligible for simplified treatment.[2,3]

Potential Pretreatment Assessments May Include:[1,4]

Assessment	Recommendation[1]	Provider Type	Invasive/ Noninvasive	Minimum Turnaround Time
HIV coinfection	All patients initiating DAA therapy should be assessed for HIV coinfection	Non-specialist/general	Noninvasive	1–2 days[5]
HBV coinfection	All patients should be tested for evidence of current or prior HBV infection before initiating treatment with DAAs	Non-specialist/general	Noninvasive	1–2 days[6]
CBC with platelets	Recommended within 6 months prior to starting DAA therapy	Non-specialist/general	Noninvasive	1 day[7]
INR				1 day[8]
eGFR				1 day[9]
CMP	Recommended within 6 months prior to starting DAA therapy	Non-specialist/general	Noninvasive	1 day[10]
Hepatic function panel Albumin ALT AST Total and direct bilirubin	Recommended within 6 months prior to starting DAA therapy	Non-specialist/general	Noninvasive	1 day[11]
Liver fibrosis assessments* *Blood tests* FIB-4 APRI FibroSure®	Evaluation for advanced fibrosis using noninvasive markers and/or elastography (ie, blood tests and imaging), and rarely liver biopsy, is recommended for all persons with HCV infection to facilitate decision making regarding HCV treatment strategy and management	Non-specialist/general	Noninvasive	Variable; 3–5 days[12]
Imaging FibroScan®		Specialist		Instantaneous
Liver biopsy METAVIR* scoring		Specialist	Invasive	1 day[13]
HCV genotyping	May be considered for those in whom it may alter treatment recommendations	Non-specialist/general	Noninvasive	3–5 days[14]
Resistance-associated substitutions†	Resistance testing is rarely used in current practice and only needed when results would modify treatment management in certain patients	Specialist	Noninvasive	10–14 days[15–17]

Assessments highlighted in purple are the AASLD recommended pretreatment assessments for patients eligible for simplified treatment.[2,3]

*Subspecialty care and consultation may be required for persons with HCV infection who have advanced fibrosis or cirrhosis (Metavir stage ≥F3).
†Recommended for select DAA treatments.[1]

Some treatment-naïve patients without cirrhosis or with compensated cirrhosis based on a previously performed cirrhosis assessment may be eligible for simplified treatment; **pretreatment assessments for these patients** may include HIV/HBV coinfection, CBC, INR, eGFR and hepatic function panel[2,3]

HBV and HIV Coinfection Assessments

Screening for other conditions that may accelerate liver fibrosis, including hepatitis B and HIV infections, is recommended for all persons with active HCV infection[1]

HBV Coinfection

Patients with chronic or resolved HBV are at risk of HBV reactivation when undergoing immunosuppression, or when receiving DAA therapy for HCV infection; therefore, all patients initiating HCV DAA therapy should be tested for HBV with HBsAg, anti-HBs, and anti-HBc[1,2]

Patients found or known to be HBsAg positive should be assessed for whether their HBV DNA level meets AASLD criteria for HBV treatment[1]

For additional information on HBV reactivation, please **click here** to access the **HBV reactivation guide**

HIV Coinfection

HIV coinfection may accelerate fibrosis progression among patients with HCV[18]

It is therefore important that all individuals with HCV infection are also screened for HIV using an HIV antibody test[1,19]

HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications; collaboration with the HIV practitioner is recommended[20]

HIV screening with reflex to confirmation: **CPT code: 87389[5] | LabCorp Code: 083935[5]**

Routine Assessments to Consider Prior to DAA Therapy Initiation

AASLD-IDSA recommend a number of routine assessments to be considered 6 months prior to initiation of DAA therapy[1]

Several noninvasive tests are recommended to assess disease progression and underlying medical conditions, including:[1,21]

CBC with platelets[22,23]

Test	Normal Range	Interpretation of Abnormal Results
Red blood cell count	4.4–5.9 x 10^6 µL	Low levels can indicate anemia Anemia can occur with advanced liver disease
Hemoglobin	12.3–17.5 g/dL	
Hematocrit	38%–47.7%	
WBC count	4,500–11,000 µL	Patients with chronic HCV may have low levels of WBC
Platelets	150,000–450,000 µL	<150,000 µL is known as thrombocytopenia and may be suggestive of cirrhosis

A reduction in platelet count, also known as thrombocytopenia, affects **6%** of patients **without cirrhosis** and **70%** of patients **with cirrhosis**[24]

INR (prothrombin time)

Test	Normal Range	Interpretation of Abnormal Results
PT (INR)	PT: 11–13.5 seconds 0.8–1.1 INR	An increase in time for blood to clot may indicate liver damage In patients with cirrhosis, prothrombin time is usually prolonged[24,25]

When the liver is damaged it may not produce sufficient levels of the main factors needed for blood clotting, causing an increase in the time it takes the blood to clot (prothrombin time)[25]

eGFR

Test	Normal Range	Interpretation of Abnormal Results
eGFR*	>90 mL/min[1]	<15 mL/min may be indicative of end-stage renal disease; no dose adjustment in DAAs is required when using recommended regimens[1]

*Calculator for eGFR: https://www.hepatitisc.uw.edu/page/clinical-calculators/mdrd.
CKD stages: 1 = normal (eGFR >90 mL/min); 2 = mild CKD (eGFR 60–89 mL/min); 3 = moderate CKD (eGFR 30–59 mL/min); 4 = severe CKD (eGFR 15–29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min).[1]

CBC with platelets	**CPT code: 85025[11] | Quest Diagnostics™ Code: 6399[21] | LabCorp Code: 005009[11]**
INR	**CPT code: 85610[12] | Quest Diagnostics™ Code: 8847[21] | LabCorp Code: 005199[12]**
eGFR	**CPT code: 82565[13] | Quest Diagnostics™ Code: 375[21] | LabCorp Code: 100768[13]**

Hepatic Function Panel

The potential liver damage caused by chronic HCV infection can be measured through an assessment of liver function using a panel of laboratory tests[20]

Hepatic functional panels typically consistent of:

AST | ALT | Albumin | Bilirubin | Platelets* | INR*

*Sometimes part of the panel

Normal ranges for hepatic function panel test results[26-28]:

Key Hepatic Function Panel Tests	Normal Range	Abnormal results
AST	AST: 8–48 U/L ALT: 7–55 U/L Typically reported as a ratio of AST/ALT of <1.0	AST/ALT >1 can indicate advanced fibrosis/cirrhosis
ALT		
Albumin	3.4–5.4 g/dL	<3.5 g/dL can indicate cirrhosis
Total Bilirubin	0.3–1.9 mg/dL	Elevated levels can be indicative of advanced liver disease, including cirrhosis

Interpretation of test results summary:

Liver condition or disease	Bilirubin	ALT or AST	Albumin	PT
Acute liver damage ie infection-, toxin-, or drug-related	Normal or increased usually after ALT/AST increases	Typically greatly increased (ALT usually higher than AST)	Normal	Usually normal
Chronic liver disease	Normal or increased	Mildly or moderately increased	Normal	Normal
Cirrhosis	May be increased at a later point in the disease	AST is typically higher than ALT; levels usually lower than in alcoholic disease	Normal or decreased	Usually prolonged

For more information on the hepatic function panel, **click here** to watch the **Assessing Hepatitis C infection: Common laboratory tests** video

Hepatic Function Panel test code: **CPT code: 322755[11] | Quest Diagnostics™ code: 34391[21] | LabCorp code: 80076[11]**

Fibrosis Assessment

AASLD-IDSA recommend the use of **noninvasive tests** to determine the level of liver fibrosis, with FIB-4 as the preferred method for the AASLD–IDSA simplified treatment algorithm[1]

Noninvasive Fibrosis Assessment

Overview of Calculations and Sensitivity of Noninvasive Liver Fibrosis Tests:*

FIB-4[27–29]

A quantitative method to estimate the level of scarring on the liver

$$\frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

FIB-4 >1.45
- 90% sensitivity
- 58% specificity

FIB-4 >3.25
- 55% sensitivity
- 92% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%:
- FIB-4 <1.45 is 97% predictive of not having cirrhosis
- FIB-4 <3.25 is 92% predictive of not having cirrhosis

A score >3.25 suggests a high likelihood of advanced liver disease (F3–F4 stage)

APRI[26–28]

A quantitative method to predict presence of fibrosis/cirrhosis

$$\frac{\dfrac{\text{AST level (IU/L)}}{\text{AST (upper limit of normal*) (IU/L)}}}{\text{Platelet count}}$$

*Usually 40IU/L

Fibrosis severity correlates with ↑ in AST level and ↓ in platelet count

APRI >1
- 77% sensitivity
- 75% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%,
APRI ≤1 is 95% predictive of not having cirrhosis

A score <1 suggests a very low likelihood of cirrhosis

FibroSure®[26,27,30,31]

A quantitative method to estimate level of liver scarring
- Calculated using six biochemical serum markers, age and gender

Score ranges from 0.00–1.00
- Corresponds to fibrosis stages F0–F4

Commercially available test: https://www.labcorp.com
- Test code: 550123

FibroSure® >0.56
- 85% sensitivity
- 74% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%,
FibroSure® <0.56 is 97% predictive of not having cirrhosis

A score >0.74 indicates cirrhosis

CPT code: 81596[12] | Quest Diagnostic™ code: 92688[21] | LabCorp code: 550123[12]

FibroScan®[27,30,31]

Noninvasive device to estimate degree of hepatic fibrosis
- Measures liver stiffness using transient elastography
- Requires ultrasound evaluation: the more rapid the ultrasound wave spreads, the stiffer the liver (expressed in kilopascals)

FibroScan® >12.5 kPa
- 87% sensitivity
- 91% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%,
FibroScan® <12.5 is 98% predictive of not having cirrhosis

A score of >12.5 kPa indicates cirrhosis

CPT code: 91200[32]

*Does not include all tests for fibrosis; online calculators are available for FIB-4 and APRI score.

Invasive Fibrosis Assessment: METAVIR

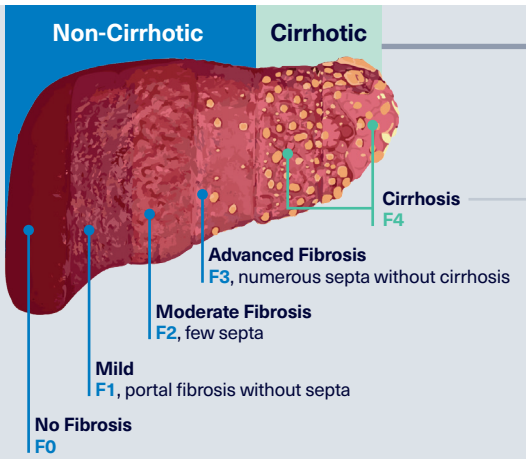
METAVIR assesses a patient's fibrosis stage (F0 to F4)* via a **liver biopsy**[33]
- It is rarely required, unless causes other than HCV infection are suspected, and is typically carried out by a specialist[29]

Click here to view the **Fibrosis and Cirrhosis Educational video 2** for more detail on fibrosis staging

Child–Turcotte–Pugh Cirrhosis Classification

Child–Turcotte–Pugh score* uses 5 clinical assessments to classify cirrhosis as compensated (CTP A) or decompensated (CTP B and C)[1]

*Online calculators are available for Child–Turcotte–Pugh score



1–5%
annual risk of HCC
(in patients with cirrhosis)[4]

Compensated cirrhosis
CTP A (5–6 points)

Decompensated cirrhosis
CTP B (7–9 points)
CTP C (10–15 points)
Patients require close monitoring and should be treated by experienced physicians.[1] Not all FDA-approved treatments for chronic HCV infection are indicated in patients with CTP B/C.

3–6%
annual risk of hepatic decompensation
(in patients with cirrhosis)[4]

Factor	Total bilirubin (mg/dL)	Serum albumin (g/L)	INR	Ascites	Hepatic encephalopathy
1 point	<2	>35	<1.7	None	None
2 points	2–3	28–35	1.71–2.3	Mild	Grade I–II (or suppressed with medication)
3 points	>3	<28	>2.3	Moderate to severe	Grade III–IV (or refractory)

Using the table to the left, points are summed to determine the CTP score

Advanced fibrosis/cirrhosis require long-term follow-up with a specialist and HCC screening. HCC screening with ultrasound is recommended every 6 months in patients with advanced fibrosis/cirrhosis regardless of treatment outcome[1]

HCV Genotypes (GT) and Resistance-Associated Substitutions (RAS)

HCV genotype may be assessed in those patients for whom it may alter treatment recommendations and can be omitted in treatment-naïve patients without cirrhosis if pangenotypic DAA regimens are available[1]

There are six common genotypes: **GT1** is the most prevalent in the United States[36]

Genotyping: **CPT code: 87902[34] | Quest Diagnostic™ code: 37811[35] | LabCorp code: 550475[14]**

RAS testing is only recommended for specific DAA regimens and *may* be assessed in those patients for whom it may alter treatment recommendations[1]

Abbreviations

AASLD
American Association for the Study of Liver Diseases
Anti-HBc
Antibody to hepatitis B core antigen
Anti-HBs
Antibody to hepatitis B surface antigen
ALT
Alanine aminotransferase
APRI
AST to Platelet Ratio Index
AST
Aspartate aminotransferase
CBC
Complete blood count
CKD
Chronic kidney disease
CMP
Comprehensive metabolic panel
CPT
Current procedural terminology
CTP
Child–Turcotte–Pugh
DAA
Direct-acting antiviral
DNA
Deoxyribonucleic acid
eGFR
Calculated glomerular filtration rate
FDA
US Food and Drug Administration
FIB-4
Fibrosis-4
GT
Genotype
HBsAG
Hepatitis B surface antigen
HBV
Hepatitis B
HCC
Hepatocellular carcinoma
HCV
Hepatitis C
HIV
Human immunodeficiency virus
IDSA
Infectious Disease Society of America
INR
International normalized ratio
IU/L
International units per liter
PT
Prothrombin time
RAS
Resistance-associated substitutions
ULN
Upper limit of normal
WBC
White blood cell

References

1. AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Last updated December 2019. www.hcvguidelines.org. Accessed July 2020
2. AASLD and IDSA. Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis. Last updated December 2019. https://www.hcvguidelines.org/treatment-naive/simplified-treatment. Accessed July 2020
3. AASLD and IDSA. Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis. Last updated December 2019. https://www.hcvguidelines.org/treatment-naive/simplified-treatment-compensated-cirrhosis. Accessed July 2020
4. CDC. Hepatitis C FAQs for Health Professionals. Last reviewed January 2020. https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed July 2020
5. HIV Antigen/Antibody Combo with Reflex to Confirmation. https://www.labcorp.com/tests/083935/hiv-antigen-antibody-combo-with-reflex-to-confirmation. Accessed July 2020
6. LabCorp. Hepatitis B Surface Antigen (HBsAg) Screen, Qualitative. https://www.labcorp.com/tests/006510/hepatitis-b-surface-antigen-hbsag-screen qualitative#:~:text=006510%3A%20Hepatitis%20B%20Surface%20Antigen,HBsAg)%20Screen%2C%20Qualitative%20%7C%20LabCorp. Accessed July 2020
7. LabCorp. Complete Blood Count (CBC) With Differential. https://www.labcorp.com/tests/005009/complete-blood-count-cbc-with-differential. Accessed July 2020
8. LabCorp. Prothrombin Time (PT). https://www.labcorp.com/tests/005199/prothrombin-time-pt. Accessed July 2020
9. LabCorp. Glomerular Filtration Rate, Estimated (eGFR). https://www.labcorp.com/tests/100768/glomerular-filtration-rate-estimated-egfr. Accessed July 2020
10. LabCorp. Metabolic Panel, Comprehensive. https://www.labcorp.com/tests/322000/metabolic-panel-14-comprehensive. Accessed July 2020
11. LabCorp. Hepatic Function Panel (7). https://www.labcorp.com/tests/322755/hepatic-function-panel-7. Accessed July 2020
12. LabCorp. Hepatitis C Virus (HCV) FibroSure®. https://www.labcorp.com/ tests/550123/hepatitis-c-virus-hcv-fibrosure. Accessed January 2020
13. LabCorp. Histopathology. https://www.labcorp.com/tests/500918/histopathology. Accessed July 2020
14. LabCorp. Hepatitis C Virus (HCV) Genotyping, Nonreflex. https://www.labcorp.com/test-menu/27426/hepatitis-c-virus-hcvgenotyping-nonreflex. Accessed July 2020
15. LabCorp. Hepatitis C Virus (HCV) NS5A Drug Resistance Assay. https://www.labcorp.com/tests/550325/hepatitis-c-virus-hcv-ns5a-drug-resistance-assay. Accessed July 2020
16. LabCorp. Hepatitis C Virus (HCV) NS5B Drug Resistance Assay. https://www.labcorp.com/tests/550505/hepatitis-c-virus-hcv-ns5b-drug-resistance-assay. Accessed July 2020
17. LabCorp. Hepatitis C Virus (HCV) GenoSure® NS3/4A. https://www.labcorp.com/tests/550540/hepatitis-c-virus-hcv-genosure-ns3-4a. Accessed July 2020LabCorp
18. Konerman MA, et al. Hepatology 2014;59:767–75
19. AASLD-IDSA Hepatitis C Guidance Panel. *Hepatology* 2020;71(2):686–721
20. AASLD and IDSA. Patients With HIV/HCV Coinfection. Last updated December 2019. https://www.hcvguidelines.org/unique-populations/hiv-hcv. Accessed July 2020
21. Quest DiagnosticsTM. Monitoring Guidance for initial treatment of HCV infection. http://questdiagnostics.solutions/dms/Documents/Other/Monitoring-Guidance.pdf. Accessed July 2020
22. LabTestsOnline. Complete Blood Count. https://labtestsonline.org/tests/complete-blood-count-cbc. Accessed July 2020
23. Hepatitis C.net. Understanding lab test results. https://hepatitisc.net/diagnosis/understanding-lab-test-results/. Accessed July 2020
24. University of Rochester Medical Center. Health Encycopedia. Albumin. https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=167&contentid=albumin_blood#:~:text=A%20normal%20albumin%20range%20is,surgery%20or%20a%20heart%20attack. Accessed July 2020
25. NIH U.S. National Library of Medicine MedlinePlus. https://medlineplus.gov/ency/article/003652.htm. Accessed July 2020
26. Lin ZH, et al. *Hepatology* 2011;53:726–36
27. Ipsos Healthcare HCV Monitor, 2017, New York, NY: Ipsos in North America
28. Chou R and Wasson N. *Ann Intern Med* 2013;158:807–20
29. Sterling RK, et al. *Hepatology* 2006;43:1317–25
30. Hepatitis C Online. Evaluation and Staging of Liver Fibrosis. http://www.hepatitisc.uw.edu/pdf/evaluation-staging-monitoring/evaluationstaging/core-concept/all. Accessed August 2020
31. Patel K, et al. *World J Gastroenterol* 2011;17:4581–9
32. Echosens. Reimbursement FibroScan®. https://echosens.us/reimbursement/. Accessed July 2020
33. Goodman ZD. *J Hepatol* 2007;47:598–607
34. Department of Health. Guide to Hepatitis C Testing. https://www.doh.wa.gov/Portals/1/Documents/5620/HCVTestingGuideForProviders.pdf. Accessed July 2020
35. Quest Diagnostics™. Hepatitis C Viral RNA, Genotype, LiPA®. https://testdirectory.questdiagnostics.com/test/testdetail/37811/?cc=AMD. Accessed July 2020
36. Polaris Observatory HCV Collaborators. *Lancet Gastroenterol Hepatol* 2017;2:161–76

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