ᏩᎳᎩ ᎠᏰᎵ
CHEROKEE NATION®

Evaluation and Treatment of Infectious Diseases in People with SUDs:

HCV Test and Treat, An Opportunity for Disease Elimination

Jorge Mera, MD, FACP

Director, Infectious Diseases

Cherokee Nation Health Services

Unintentional Bias Disclosure

- I am aware that despite my best intentions and efforts toward reducing bias and stigmatizing terms, language is evolving, and I may not be aware that certain terminology may be offensive to participants.

- I welcome your feedback on language, images, or concepts that may be offensive or stigmatizing so that I may continue to optimize my presentations.

Objectives

At the end of this presentation, participants will be able to:

- **Understand the evaluation of PWID**
- **Apply POC HCV RNA testing**
- **Review AASLD simplified HCV Test-and-Treat**
- **Identify treatment and follow-up steps**

The Connection Between Substance Use Disorders and Infectious Diseases

Under the influence of substances people are more likely to:

- Have anal or vaginal sex without protection
- Have sex with multiple partners
- Trade sex for money or drugs

Sharing needles:

- Is the second riskiest behavior for getting HIV
- Is the first riskiest behavior for getting HCV

An HIV negative person has a 1/160 chance of getting HIV

- Every time they use a needle used by someone with HIV
- HIV PrEP can decrease the risk by 70%

https://www.cdc.gov/hiv/basics/hiv-transmission/injection-drug-use.

Infectious Diseases Associated with SUD

- **Viral infections (bloodborne)**
  - Hepatitis C Virus (HCV)
  - Hepatitis B Virus (HBV)
  - Hepatitis A Virus (HAV)[4]
  - Human Immunodeficiency Virus (HIV
- **STI's**
  - Gonorrhea/Chlamydia, Syphilis
  - HIV/HCV/HBV
- **SSTI and bone Infections**
  - Cellulitis, abscesses, necrotizing fasciitis
  - Wound botulism
  - Osteomyelitis
- **Systemic infections**
  - Bacteremia, endocarditis, brain abscesses, pulmonary septic emboli

- **Injection Drug Use accounts for:**
  - HIV
    - ~9% of new cases in general population [1]
    - ~43% in AI/AN women who inject drugs
  - HCV
    - 66% of HCV cases [2]
- **Among people who inject drugs**
  - Each year ~ 20-30% will acquire HCV [3]
- **Co-infections**
  - Among injection drug users who have HIV coinfection with HCV is common (62%–80%)
  - Among PLWHIV w/o IDU, 21% have HCV [4]

1. Centers for Disease Control and Prevention, 2020. HIV Surveillance Report, www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2020-updated-vol-33.pdf 2. Centers for Disease Control and Prevention, 2016, Surveillance for Viral Hepatitis – United States, 2016. https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm 3. Grebely, J. et al. 2011. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3072734/ 4.MMWR Morb Mortal Wkly Rep 2018;67:1208–1210. DOI: http://dx.doi.org/10.15585/mmwr.mm6743a3

Bacterial Infections Associated With Substance Use Disorders, Large Cohort of United States Hospitals, 2012–2017

Hospitalizations of persons with SUDs and infections increased

- **Infectious endocarditis**: From 1.6 to 3.6 per 100 000 persons for adults aged 18–44 yo
- **Osteomyelitis:** From 1.4 to 2.4 per 100 000 persons
- **CNS abscess:** From 0.5 to 0.9 per 100 000 persons
- **SSTI:** From 24.4 to 32.9 per 100 000 persons

Conclusions

- Rates of hospitalization for serious infections among persons with SUDs are increasing, driven primarily by younger age groups.

Clinical Infectious Diseases, Volume 71, Issue 7, 1 October 2020, Pages e37–e44

Infectious Endocarditis (IE) in People Who Inject Drugs (PWID)

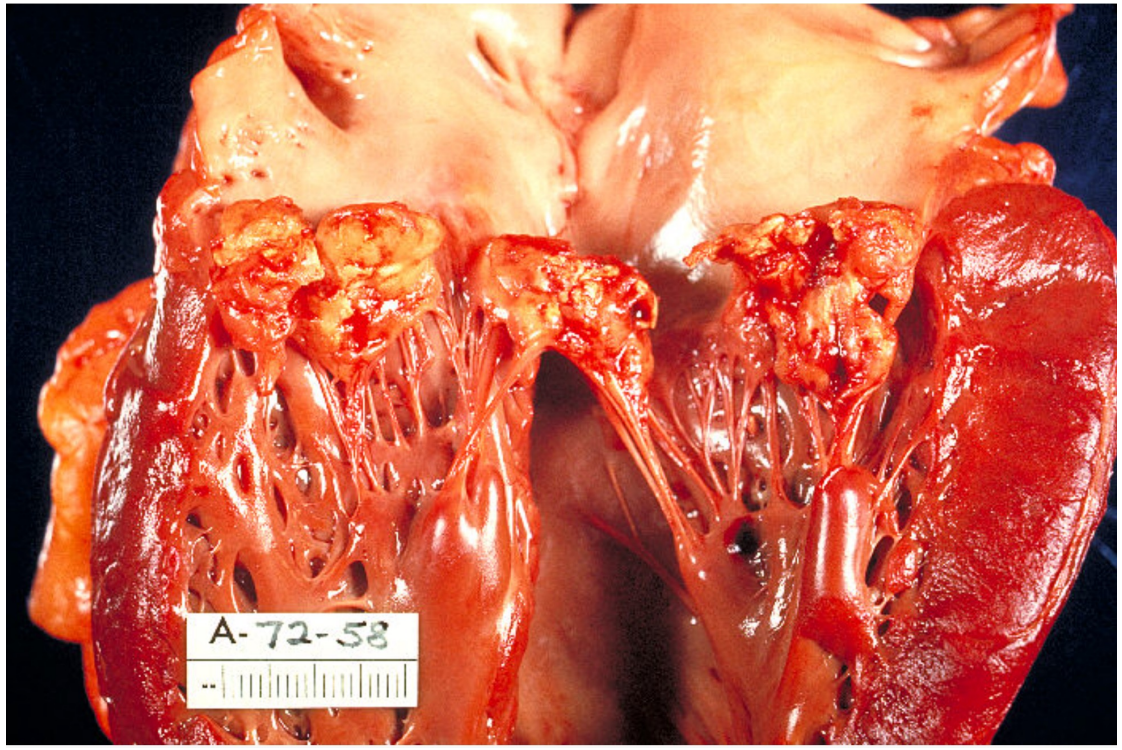
Worse outcomes compared to people who do not inject drugs

- Surgeons are hesitant to operate due to poor outcomes, substance use, and limited care.

Fentanyl use linked to

- Higer injection frequency: Injecting 6-10 times/day compared to 3-4 times/day with heroin
- Higher needle sharing which increases infectious risk.

Both increase infection transmission risk!!



https://phil.cdc.gov/Details.aspx?pid=851

Harvey L, Boudreau J, Sliwinski SK, et al. Open Forum Infect Dis. 2022 Jan 6;9(2):ofab631

What Can We Do About IT?

Prevention

- Vaccination
- Harm reduction
  - HIV PEP and PrEP
  - Safe injection education
  - Syringe Service Program
  - Medication Assisted Treatment
  - Behavioral health assessment or referral

Diagnosis

- Periodic infectious disease screening

Prevention

- **Does the patient need vaccination?**
  - HPV, Hepatitis A and B, Pneumococcal , TdAP, Shingles, COVID-19, Influenza, MPox
- **Does the patient meet criteria for HIV PrEP?**
  - Injection drug use? sharing injection equipment? Having sex when using drugs? Condom use?
- **Any sings of active infection?**
  - Physical Exam: Soft tissue infections? Heart murmurs (endocarditis?)
- **Screening**
  - Hepatitis A, B and C, HIV, Syphilis and GC/Chlamydia screening

First Encounter with People with SUD

Focus on the reason for the visit but do not limit it to that only

- **TEAMWORK:**
  - **Clerck:** empathy, retention
  - **Medical assistant:** Checks vaccine and STI screening needs
  - **Nurse:** Performs mental health screen (PHQ2, NIDA score, PoC testing (HCV, HIV, Syphilis)
  - **Provider:** Screens for HIV PrEP, addresses mental health and SUD issues (does the patient require MAT?

Second Visit: Clinical Follow-up and Review Labs and Act

Test	Result	Interpretation	Action
Hepatitis B	HBsAb (-), HBsAg (-), HBcAb (-)	Never exposed	Vaccinate
	HBsAb (+), HBsAg (-), HBcAb (-)	Immune	None needed
	HBsAb (-), HBsAg (+), HBcAb (+)	Active Infection	Refer to ID*
	HBsAb (-), HBsAg (-), HBcAb (+)	Isolated HB core Ab	Call ID
Hepatitis C	Positive HCV Ab	Possible current infection	HCV RNA*
	Positive RNA	Current Infection confirmed	Treat
Hepatitis A	Total Ab (+)	Immune	Non needed
	Total Ab (-)	Not immune	Vaccinate
G/C	Reactive	Active Infection	Treat*
Syphilis	Reactive	Active Infection	Stage and Treat *

ID: Infectious Diseases
* Evaluate for PrEP

How often should labs be ordered in people with SUD Who Inject Drugs?

Test	Result
Hepatitis C	Most guidelines recommend periodic testing but here is limited evidence to determine how often to screen persons at increased risk
Hepatitis A	Once since if negative vaccination should be offered
Hepatitis B	Once since if negative vaccination should be offered If chronic HBV present refer to specialist
GC/Chlamydia/Syphilis	Every 6 months if they are on PrEP and anytime unprotected sexual exposure is reported

PWID: People Who Inject Drugs

How Can We Mitigate This Problem?

Harm reduction

- Vaccination
- HIV PEP and PrEP
- Safe injection education
- Syringe Service Program
- Medication Assisted Treatment
- Behavioral health assessment or referral

Diagnosis

- Periodic infectious disease screening
- Use PoC when available
- Test and treat

Six Moments of Infection Prevention in Injection Drug Use: An Educational Toolkit for Clinicians

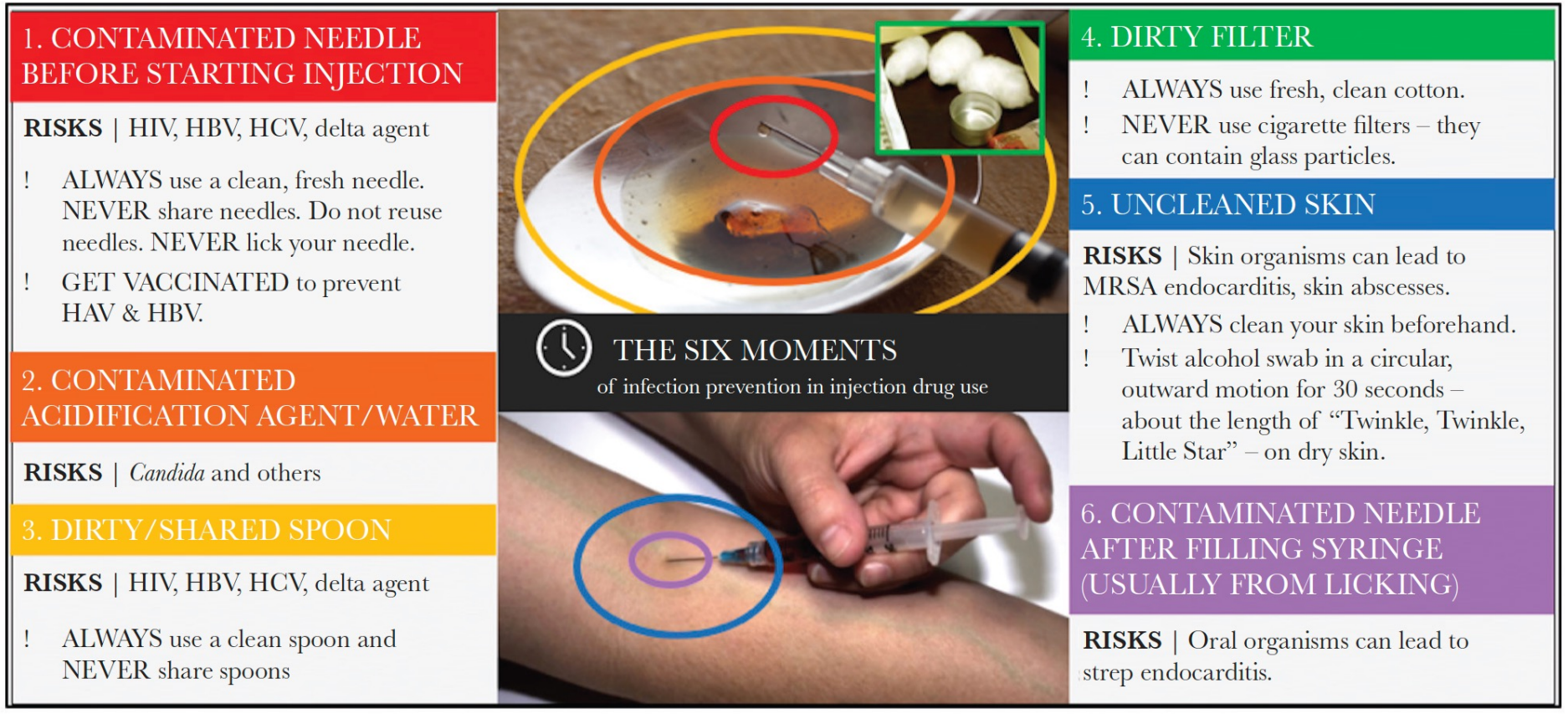


Figure 1. Six Moments of Infection Prevention in Injection Drug Use Model. Abbreviations: HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*.

Preventing Bacterial Infections

Harm reduction strategies are important tools for preventing infections in PWID.

- Access to SSPs, safe injection facilities, skin cleaning and safe injection strategies

Safe injection techniques can reduce incidence of infectious endocarditis by over 90%,

- Significantly higher than is achievable with a reduction in injection frequency alone.

SSPs reduce disease transmission by

- Decreasing the rate of needle and syringe sharing
- Reducing needle reuse and the length of time that used injection materials are in circulation

Harvey L, Boudreau J, Sliwinski SK, et al. Open Forum Infect Dis. 2022 Jan 6;9(2):ofab631

Clinical Vignette

HPI: 42-year-old man with a **PMHx significant for SUD only** comes as a walk-in patient to your clinic asking for information about syringe service programs. He injects drugs twice daily, mainly heroin. He sometimes shares needles, last time he shared was 2 weeks ago. You offer him buprenorphine/naloxone induction, but he is not ready yet

PE: Except for track marks in his arms his physical exam is otherwise normal

POC testing reveals **negative** T. pallidum, HIV Ab/Ag, and **HCV antibody**
Your savvy medical assistant performs a **POC HCV RNA** and this is **POSITIVE**

Clinical Vignette

How do you interpret these results?

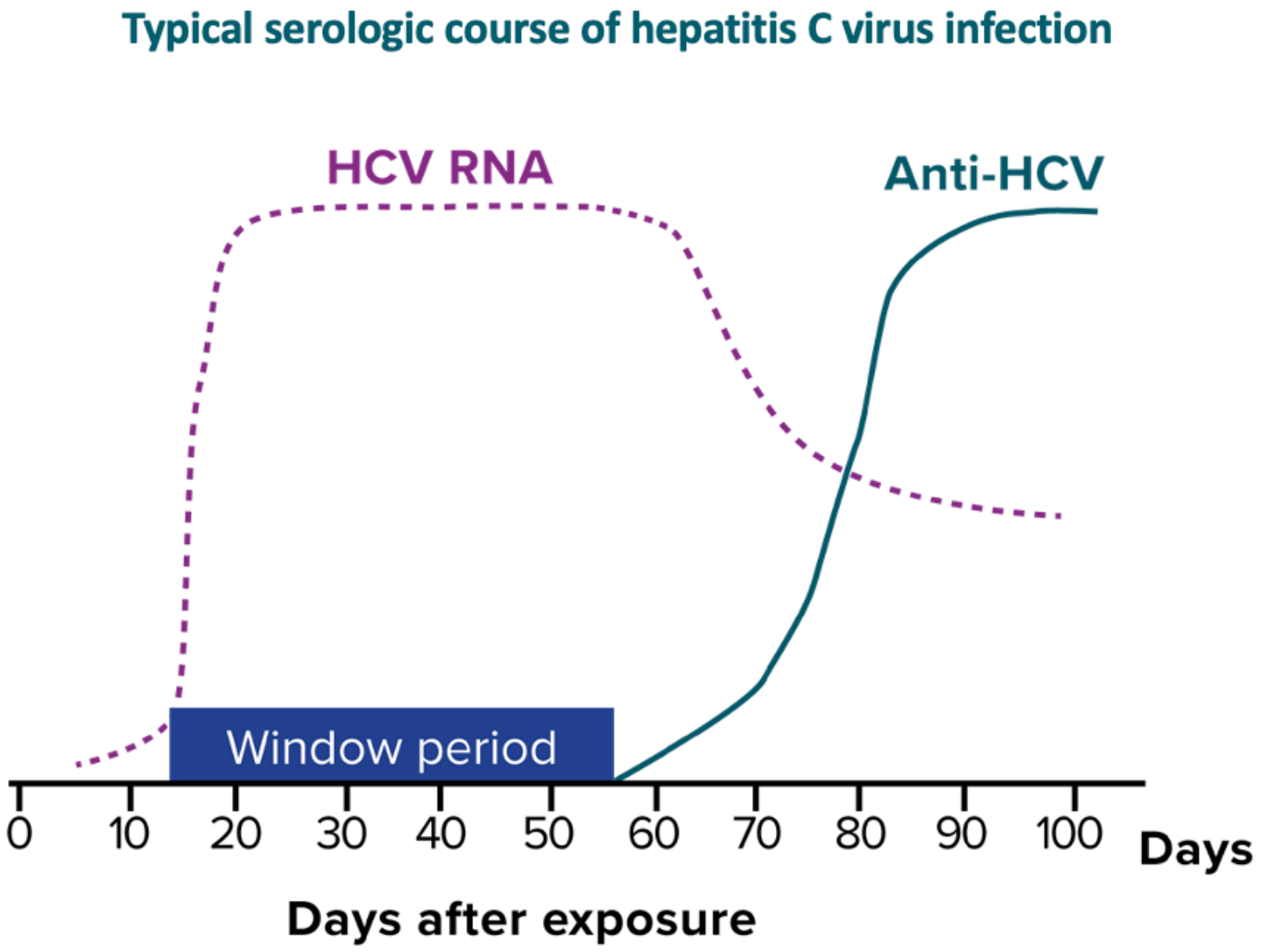
A. The patient has occult hepatitis C infection with selective antibody non-response

B. The patient has acute hepatitis C infection during the window period before antibody seroconversion

C. The HCV RNA test is a false positive and should be disregarded given the negative antibody test

D. The tests are discordant due to laboratory error and both should be repeated immediately

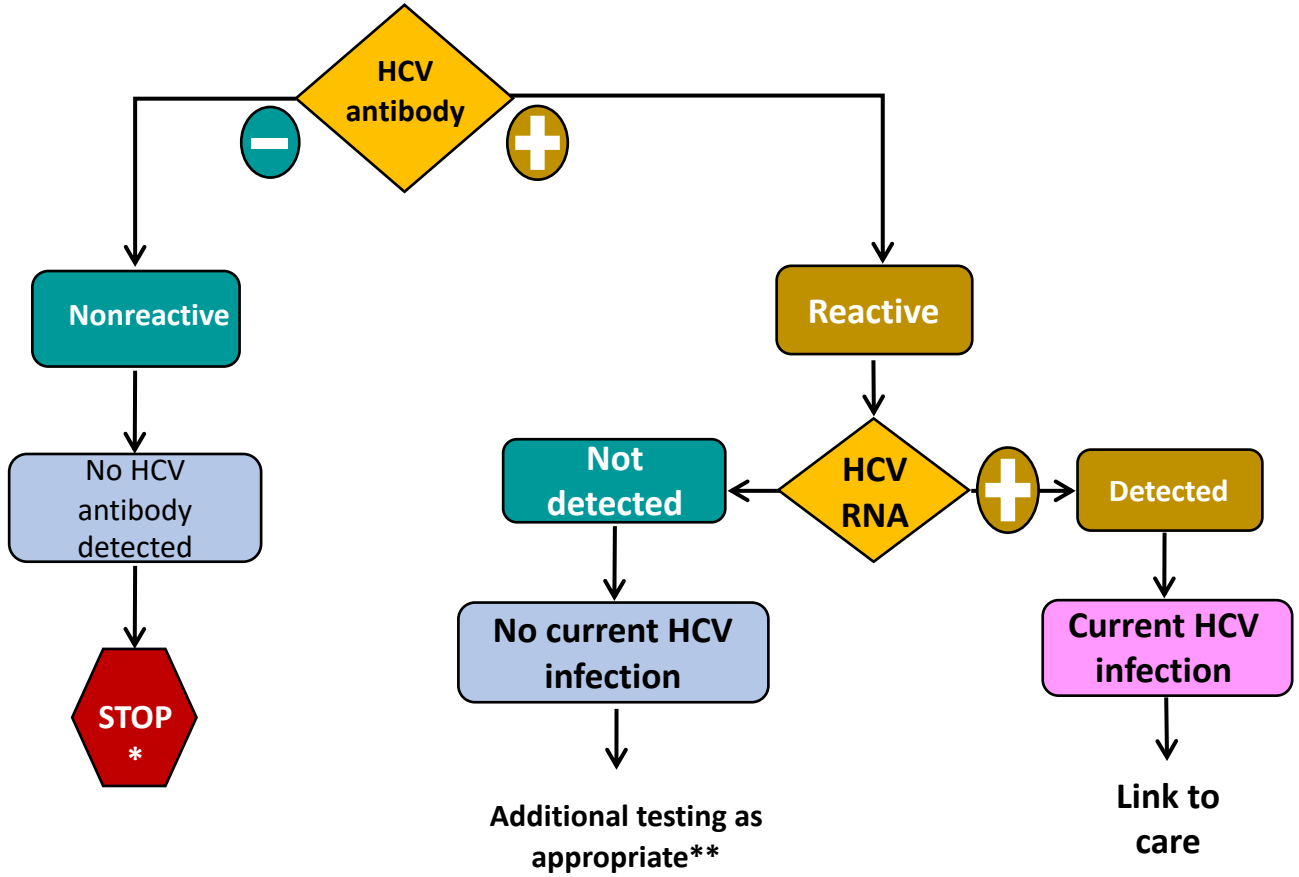
False Negative HCV Antibody



CDC HCV Screening Recommendations:

SOURCES: CDC Recommendations for Hepatitis C Screening, MMWR, April 2020
CDC Vital Signs, April 2020

Schillie S, Wester C, Osborne M, Wesolowski L, et al. MMWR Recomm Rep 2020;69(No. RR-2):1–17.



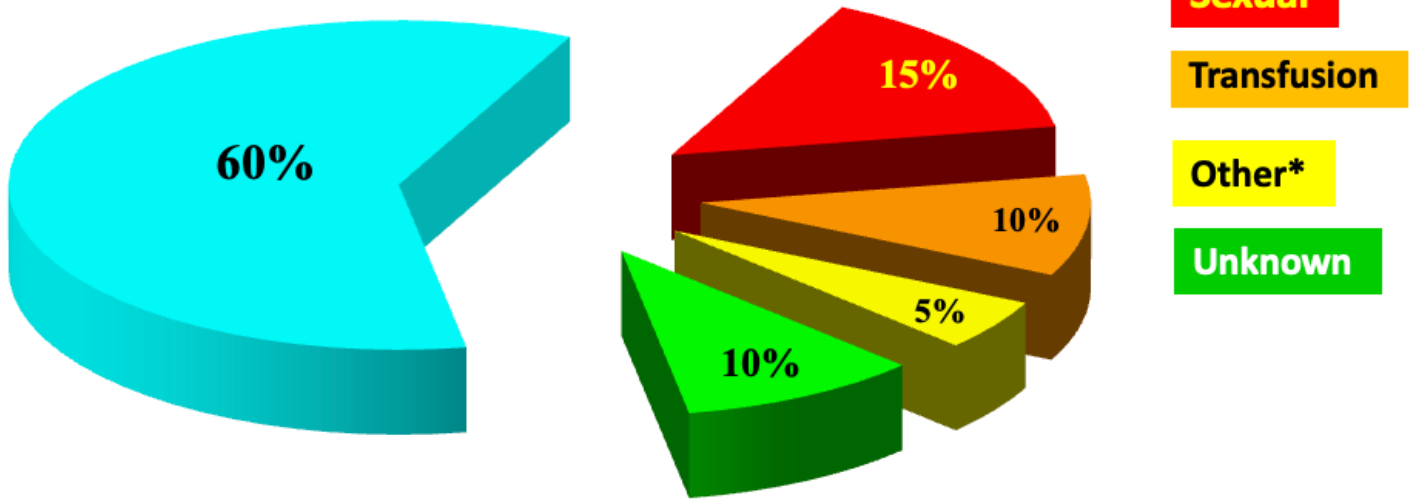
* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.
** To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen. CDC. Testing for HCV infection. *MMWR*. 2013;62(18).

HCV: Transmission

- **Blood**
  - IVDU is the leading cause in the United States
    - Snorting
  - Percutaneous injuries
  - Dental
  - Tattooing
  - Blood transfusion (Before 1992)

- **Sexual contact**
  - Rare in heterosexual
  - More frequent in HIV + MSM

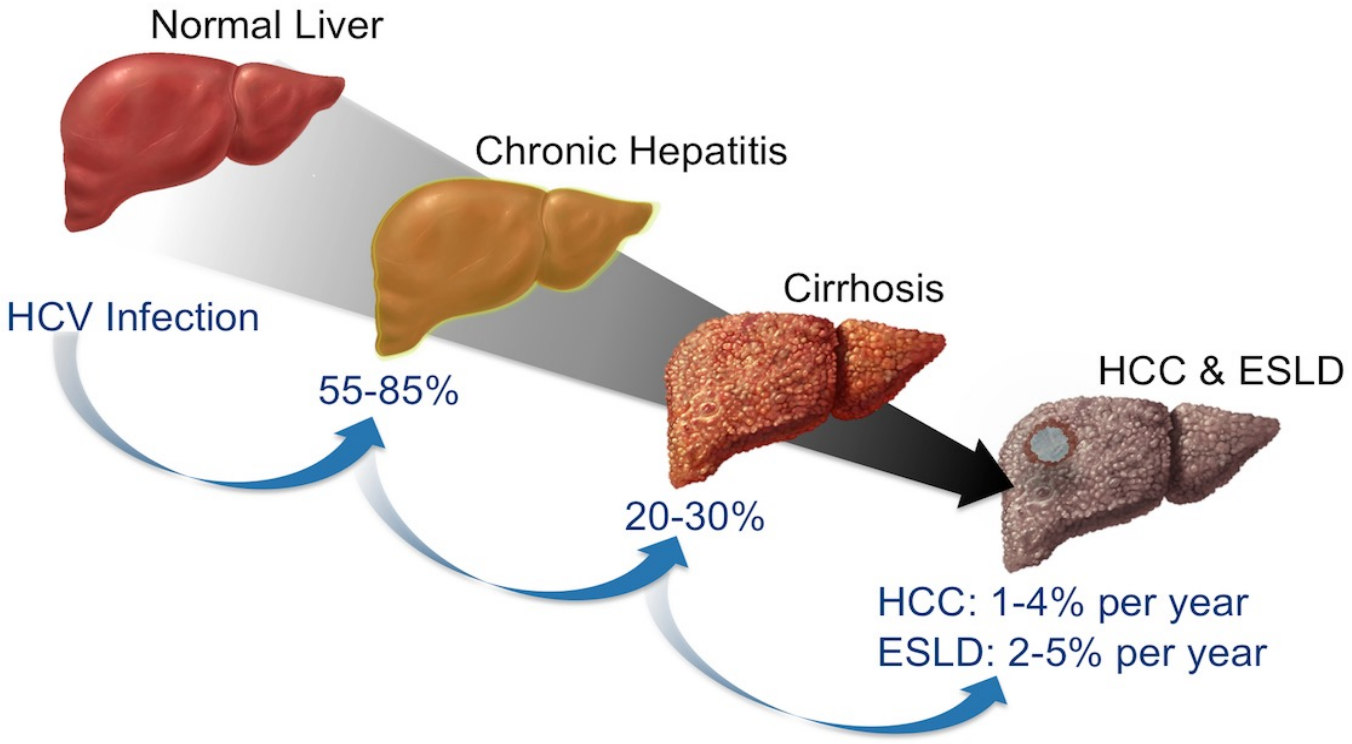
- **Mother-to-child**
  - The rate is 1.7% - 4.3 %
  - *Increased in IVDU, HIV co-infection, VL (?)*



*Nosocomial; Health-care work; Perinatal

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance—United States, 2016. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2018. Available at: https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm.

Natural History Following Initial HCV Infection



Rates of progression to cirrhosis are increased in the presence of a variety of factors, including:

- Being male
- Being age >50 years
- Consuming alcohol
- Having nonalcoholic fatty liver disease, hepatitis B, or HIV coinfection
- Receiving immunosuppressive therapy[1,2,3]

Abbreviations: ESLD = end-stage liver disease HCC = hepatocellular carcinoma

Clinical Vignette

According to the AASLD guidelines, what is the next step?

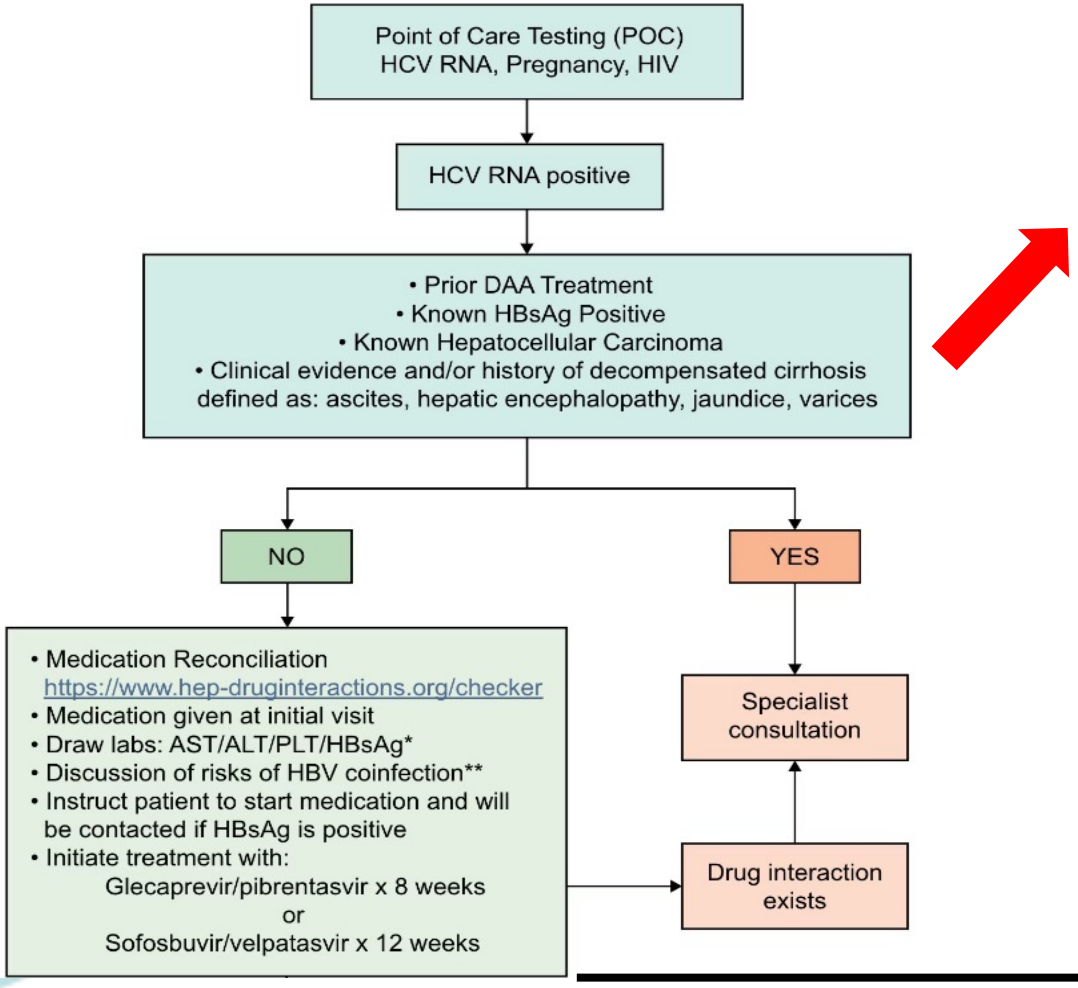
A. Draw blood and send out for HCV RNA confirmation an HCV Genotype

B. Draw blood for Hepatitis B serologies, CBC, CMP and start HCV treatment

C. Draw blood for Hepatitis B serologies, CBC, CMP and wait for results before starting treatment

D. The patient does not need any other lab work, start HCV treatment

AASLD Guidelines
Hepatitis C Test and Treat Initial Visit



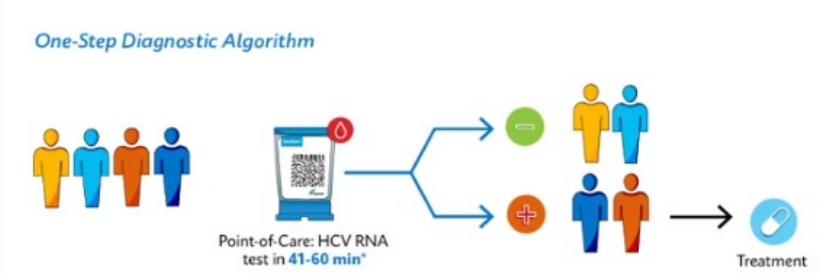
Screening for rapid treatment start:

1. Ever treated before for HCV?
2. Have you ever been told you had chronic hepatitis B?
3. Have you been diagnosed with liver cancer?
4. Have you ever vomited blood? If yes, do you know what caused it?
5. Have you ever been diagnosed with hepatic encephalopathy?
6. Where you ever told you had fluid on your belly?
7. Do you have swelling on both feet?

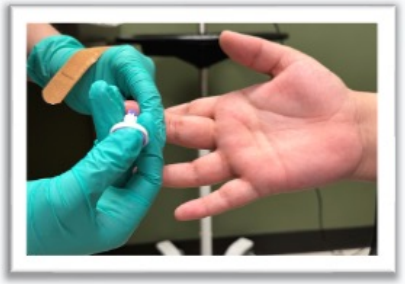
Hepatitis C Virus Diagnosis

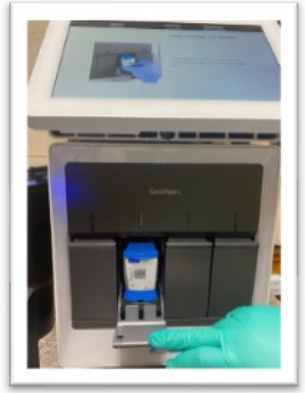
Test Name	Clinical Utility	Turnaround Time
HCV antibody (POC)	For screening	**30 minutes**
HCV antibody Reflexed to HCV RNA (lab based)	Reflex test for screening and confirming active infection	**1-4 days**
HCV quantitative RNA (POC)	For confirmation of active infection	**45-60 minutes**

HCV RNA Point of Care HCV Testing*



Cepheid's Xpert® HCV, June 27, 2004





*https://www.cepheid.com/en-US/tests/blood-virology-womens-health-sexual-health/xpert-hcv-info.html

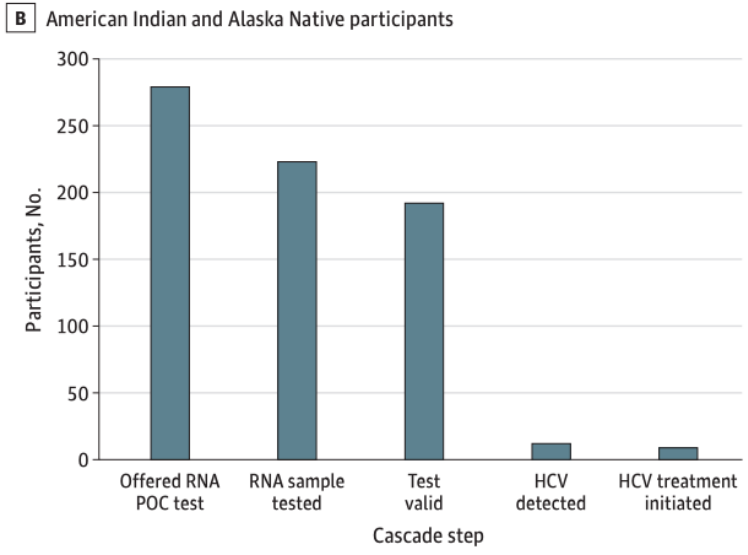
Hepatitis C Virus Diagnosis

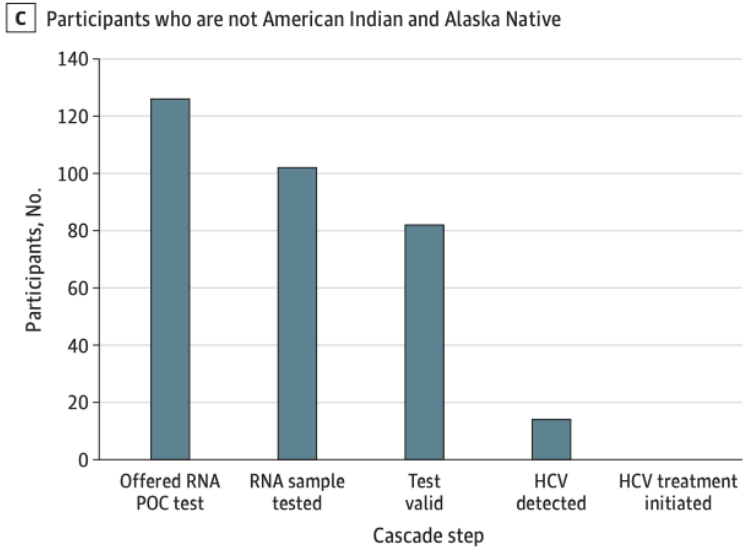
JAMA Network Open

Original Investigation | Infectious Diseases

Point-of-Care Hepatitis C Testing in a Tribal Setting

Jorge Mera, MD; Andrea Blair, PhD; Kendra Lewis, MHA; Savana Christy, BS, MLS(ASCP)CM; Molly Feder, MPH; Ashley Comiford, DrPH





Key Points

Question Is it feasible to implement point-of-care hepatitis C virus (HCV) RNA testing and same-day treatment in a tribal setting, including a harm reduction site?

Findings In this quality improvement study, 405 point-of-care HCV RNA tests were offered, 86% were accepted, and 79% yielded valid samples; HCV was detected among 26 valid samples. Of the samples with HCV, 12 were from American Indian and Alaska Native participants: 9 initiated treatment, 6 the same day, whereas no participants who were not American Indian and Alaska Native initiated treatment.

Meaning This study suggests that a community-based point-of-care HCV RNA testing program was feasible and was associated with a high percentage of same-day treatment for American Indian and Alaska Native participants.

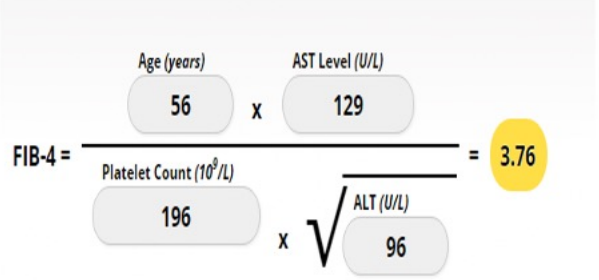
Most Patients Are Treatable in Primary Care

- **Substance use is not a contraindication**

- **Pretreatment labs needed**
  - Results can be deferred
  - **HBsAg !! May require treatment if positive**
  - Hep A total Ab or IgG, HBsAb, HBcAb. Important for **evaluating vaccination**
  - Platelet count, AST and ALT. Important for evaluating presence of cirrhosis
    - FIB-4 > 3.25 or a platelet count < 150,000/m^3 **suggest cirrhosis**

Non-Invasive Liver Fibrosis Staging in the Office

FIB–4 Index



A FIB-4 score <1.45 has a negative predictive value of 90% for advanced fibrosis A FIB-4 >3.25 has a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Lin ZH, Xin YN, Dong QJ, et al. Hepatology. 2011;53:726-36
Sterling RK, Lissen E, Clumeck N, et. al. Hepatology 2006;43:1317-1325
University of Washington: Hepatitis C Online www.hepatitisc.uw.edu/

Simplified Pre-Treatment Assessment

Medication reconciliation:

- Record current medications, including over-the-counter drugs and herbal/dietary supplements.

Potential drug-drug interaction assessment:

- Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.

Education:

- Educate the patient about proper administration of medications, adherence, and prevention of reinfection.

https://www.hcvguidelines.org/

Recommended Treatment Regimens

Mavyret: Glecaprevir (300 mg) / pibrentasvir (120 mg) to be taken with food for a duration of 8 weeks

Epclusa: Sofosbuvir (400mg0/velpatasvir (100) mg for a duration of 12 weeks

Monitoring

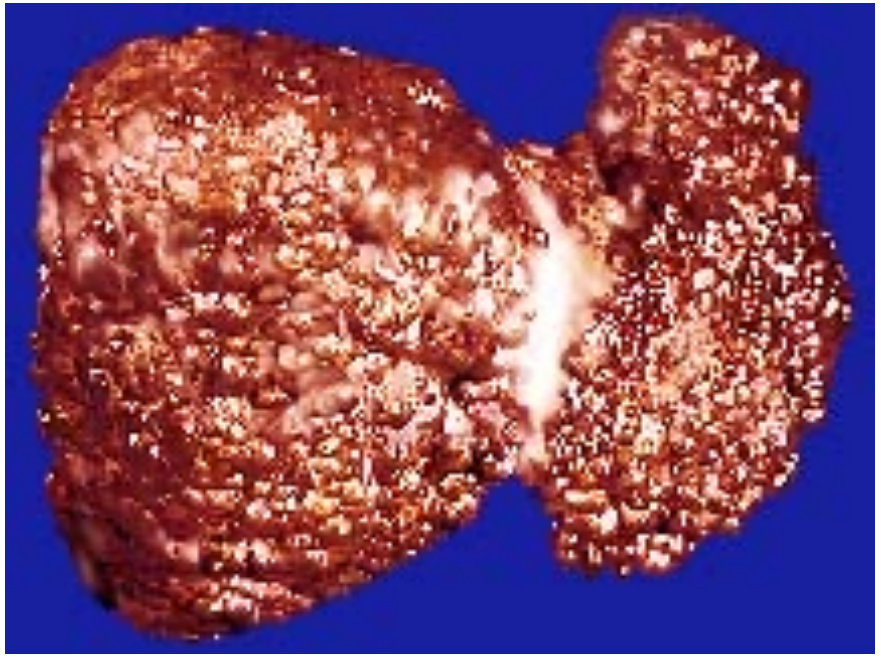
- No laboratory or clinical monitoring is required for the majority of patients
- **Monitor for hypoglycemia** In diabetic patients
- **Monitor INR** in patients taking warfarin
- Consider in-person or telehealth/phone visit if needed for patient support

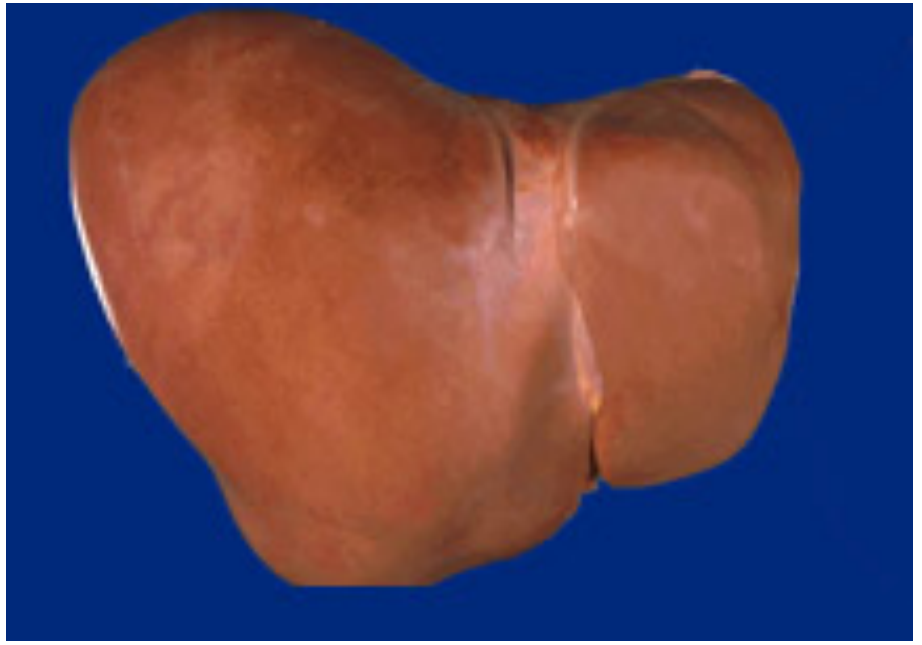
NOTE: Patients with cirrhosis who are being treated with sofosbuvir/velpatasvir will require a genotype, since if the patient has a genotype 3 baseline NS5A resistance-associated substitution (RAS) testing will be required.

https://www.hcvguidelines.org/

What Does HCV Treatment and Cure Accomplish?

- 70% Reduction of Liver Cancer
- 50% Reduction in All-cause Mortality
- 90% Reduction in Liver Failure





NOTE: Patients with cirrhosis who are being treated with sofosbuvir/velpatasvir will require a genotype, since if the patient has a genotype 3 baseline NS5A resistance-associated substitution (RAS) testing will be required.

https://www.hcvguidelines.org/

Helpful Resources

http://www.npaihb.org

Text HCV 97779

http://www.hcvguidelines.org/

http://www.hepatitisc.uw.edu/

On-line curriculum on liver disease and HCV, includes clinical studies, clinical calculators, slide lectures

ProjectECHO HCV guidelines

Thank You