

Treating Hepatitis C among people who use drugs



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Disclosures

None



Objectives

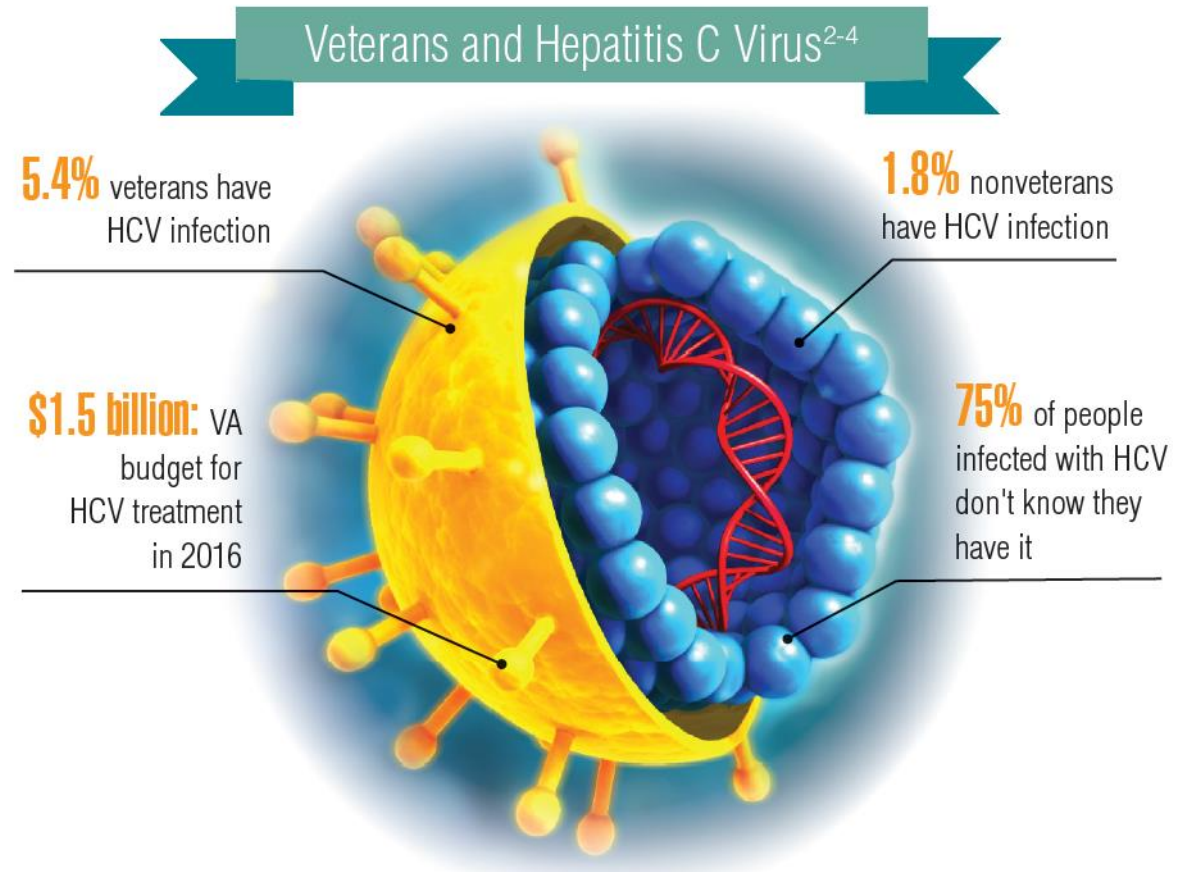
- Provide an overview of the HCV
- Review epidemiology and USPSTF recommendations for screening
- Discuss routes of transmission
- Review natural history of HCV and alcohol effects
- Discuss benefits of cure
- Review recommendations for treatment
- Discuss consequences of not treating HCV
- Emphasize the simplicity of treatment in most patients
- Review the role of Ultrasonography in patients with fibrosis/cirrhosis
- Discuss the importance of vaccination for HAV and HBV
- Discuss HBV/HCV co-infection
- Discuss misconceptions in treating HCV in those that use drugs



Hepatitis C virus

- RNA virus identified in 1988
- *Not vaccine preventable*
- Majority of people exposed to HCV will develop chronic infection (approximately 20% will clear the virus spontaneously)
- Most common blood-borne infection in US

Among adults in the U.S., the most common reason for a **liver transplant is chronic hepatitis C**

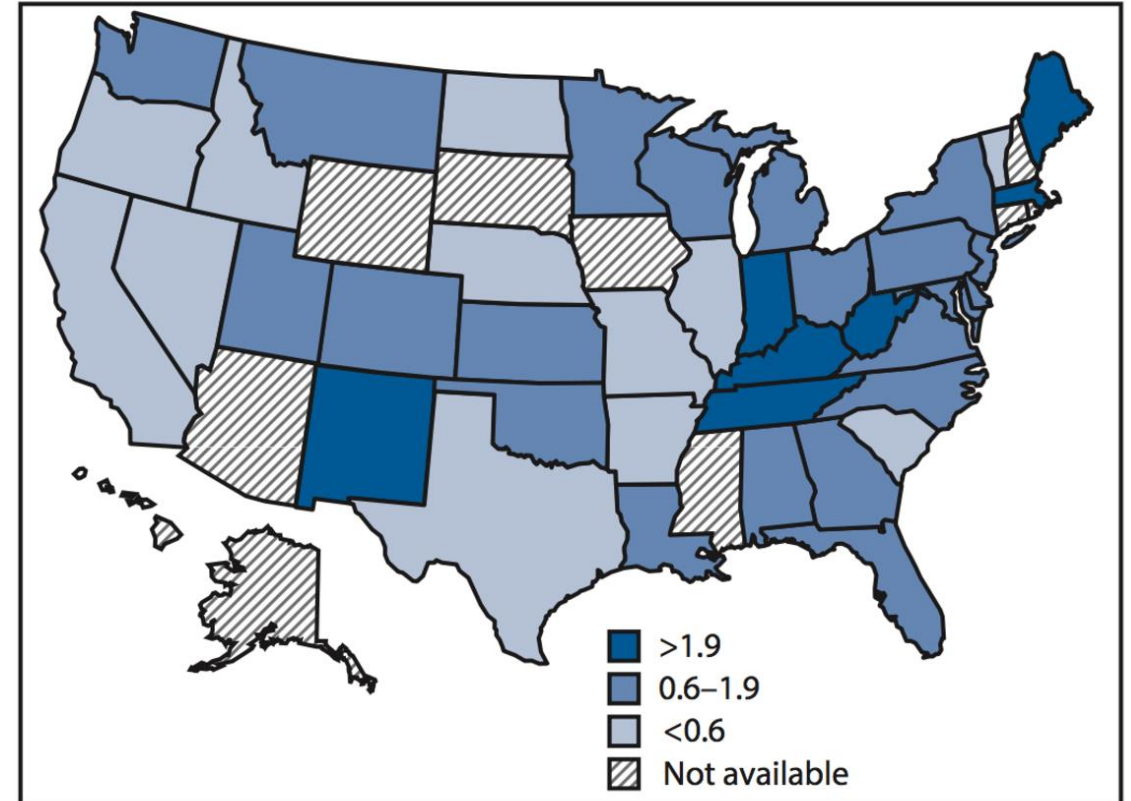


Hepatitis C incidence

Deadly virus

- Many persons with HCV (~1/2) are unaware of their infection
- In U.S., deaths from HCV outnumber those from HIV plus 60 other infectious conditions combined

FIGURE 1. Acute hepatitis C virus infection incidence rate ratios* — United States,[†] 2015



* The national rate (0.8 per 100,000 population) is the denominator.

[†] Seven states have rates at least twice the national average: Indiana, Kentucky, Maine, Massachusetts, New Mexico, Tennessee, and West Virginia. Ten states have rates above the national average (but not twice the national average): Alabama, Montana, New Jersey, North Carolina, Ohio, Oklahoma, Pennsylvania.



Hepatitis C and HBV co-infection

- Worldwide, about 170 million people have hepatitis C, while about 2.4 million Americans are infected. It is the leading cause of liver cirrhosis and liver transplants in the United States
- AASLD recommends starting people with HBV/HCV coinfection, who meet the criteria for treatment of active HBV infection, on therapy at the same time ***or before starting direct acting antiviral (DAA) for HCV treatment. At this point, treatment of HBV is not curative and long term.***

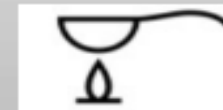
HCV in the U.S.: Routes of Transmission

- **Injection drug use: majority of cases**
- Blood transfusion prior to 7/1992
- Receipt of solid organ transplantation or factor concentrates made before 1987
- Healthcare exposure
- Sex (especially male-to-male sex)
- Unregulated tattoos
- Maternal-child transmission
- Sharing personal items in contact with blood



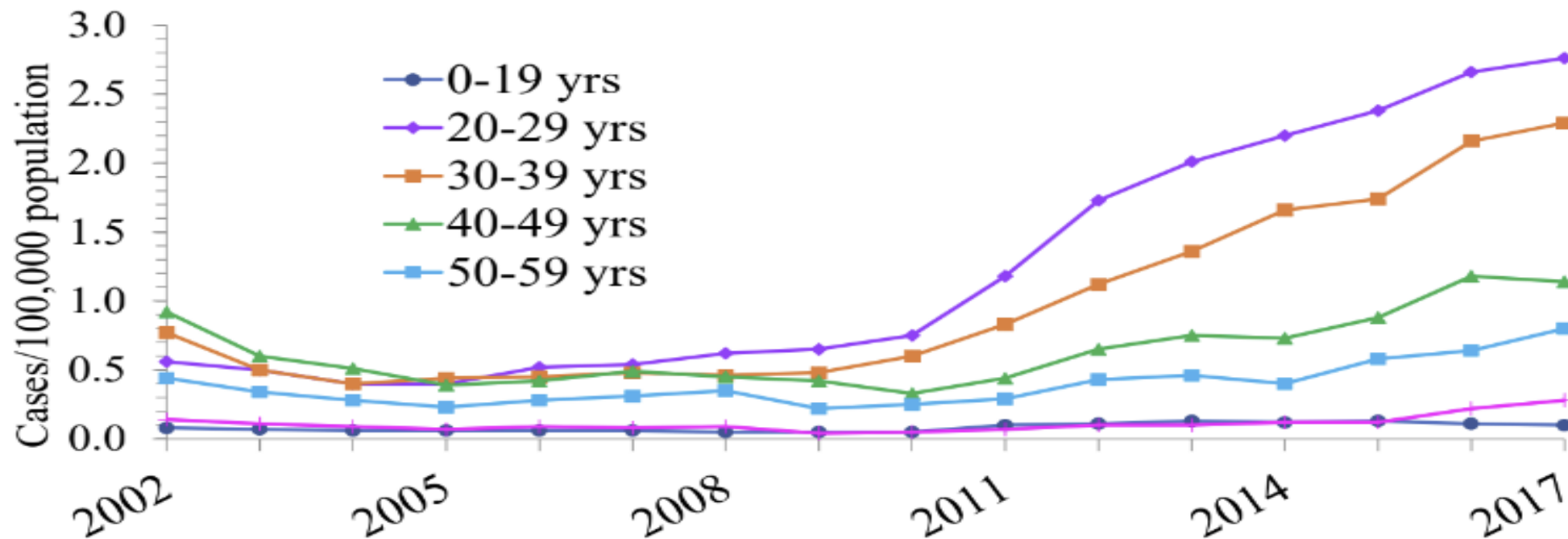
Highest risk: sharing needles
and syringes

Can also occur with sharing
injection paraphernalia such as
water, cookers, and cotton filters



Opioid Epidemic and HCV

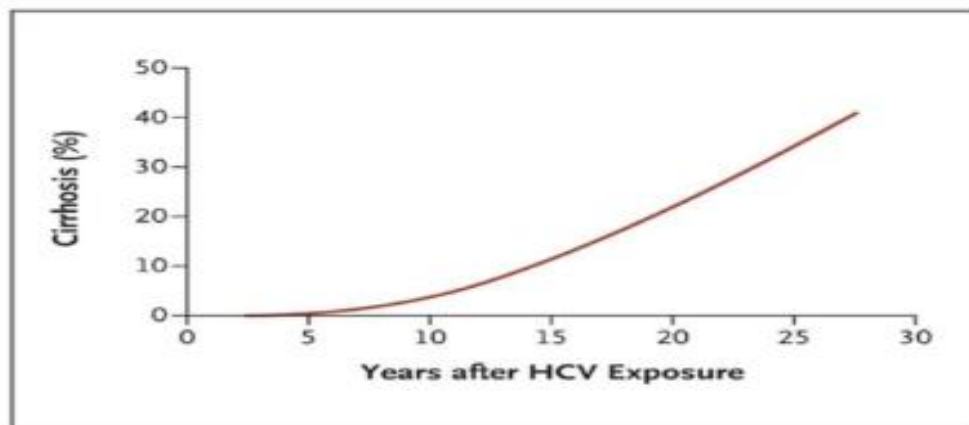
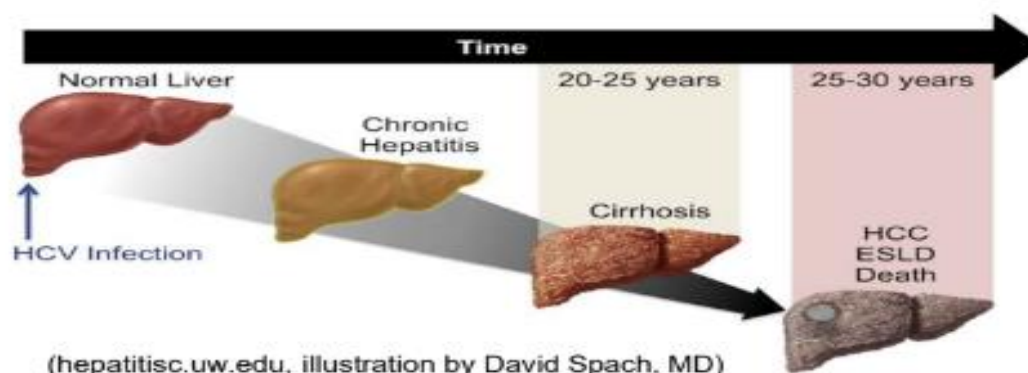
- **Emerging epidemic** of HCV among young people who inject drugs (PWID)
- Closely related to opioid crisis



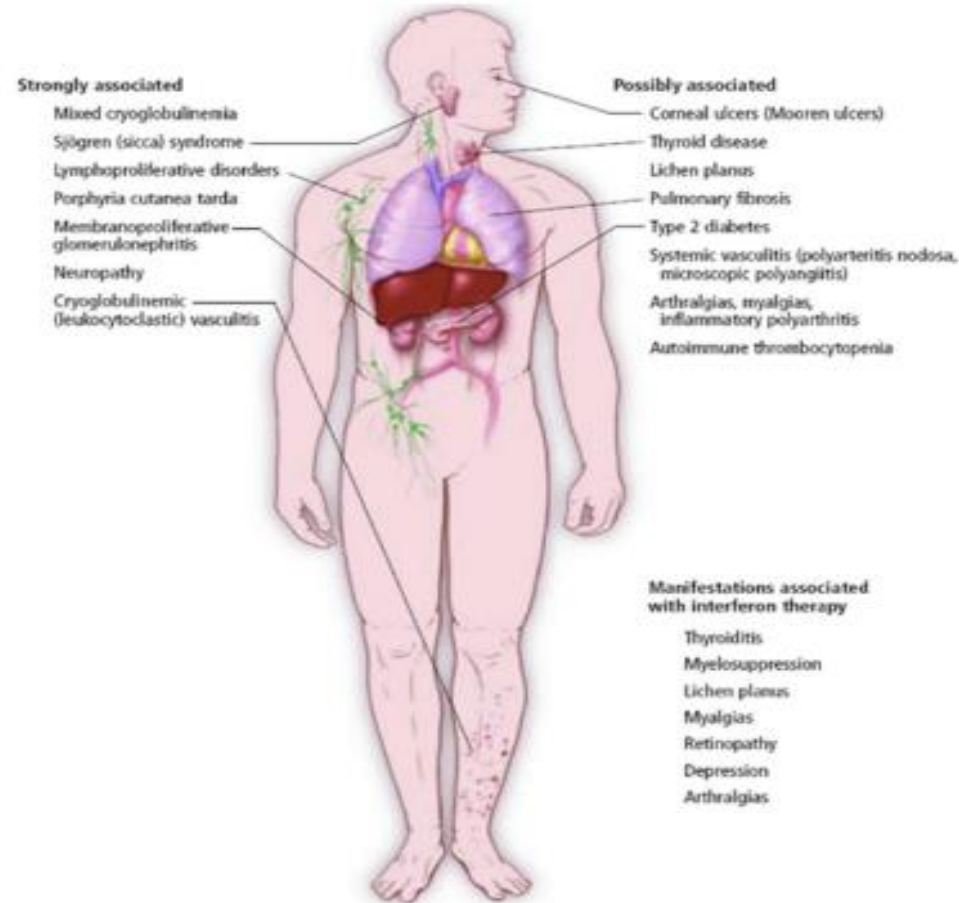
Rates of reported acute hepatitis C by age group, US, 2002-2017 (CDC Viral Hepatitis Surveillance Data)

Natural History of Chronic HCV

- 15-30% of those with chronic HCV will develop cirrhosis, which can lead to:
 - Hepatocellular carcinoma (3-5% incidence per year)
 - Liver failure
 - Death
- Alcohol use increases each of these risks AND affects transplant candidacy



Lived Experience with HCV



- Symptoms: range from none at all to systemic, hepatic, and a variety of extra-hepatic symptoms
- Patients frequently report fatigue, sleep problems, depression, and anxiety¹
- Stigma and illness-related uncertainty contribute to chronic stress²

Benefits of Cure of HCV

Reduced all-cause
mortality

Positive psychosocial
effects and improved
quality of life

Reduction in liver
fibrosis and liver
complications

Reduced
transmission to
others

Reduced incidence
of liver cancer

Decreased
inflammation and
non-hepatic
comorbidities

Treatment is also prevention

Treating populations that actively transmit HCV reduces new infections



What patients with HCV should be treated?

- Nearly everyone:

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING ⓘ
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

- What about people who use drugs?

★ To eliminate HCV, treating people who use drugs is **critical** ★

Misconceptions

#1 People who use substances can't be effectively treated / cured

#2 People who use substances are most likely to get reinfected anyway

- Though previously assumed true and incorporated into guidelines and coverage requirements, these assumptions have been largely disproven...

A scientist in a white lab coat and blue gloves is working in a laboratory. They are using a pipette to transfer a small amount of green liquid into a petri dish. A microscope is visible in the foreground, and the background is slightly blurred, showing other laboratory equipment.

Terminology

- Cure of HCV = Sustained Virologic Response (aka SVR)
No detectable HCV virus (HCV RNA) at 12 or more weeks after completion of treatment
- DAA= direct-acting antiviral medication (to treat hepatitis C infection)

Misconception # 1

People who use substances can't be effectively treated / cured


- Studies from various settings show **good adherence** and **high cure rates** among people who use drugs, including those with injection drug use
- There are **NO data to support pretreatment screening** for illicit drug or alcohol use to select a population more likely to be successful with hepatitis C treatment, or to impose criteria for abstinence.

Studies Show High Cure Rates in PWUD

Population	Outcome
CO-STAR ¹ : 301 persons in treatment for OUD (methadone and buprenorphine) treated with elbasvir/grazoprevir	91.5% rate of SVR, no difference in adherence or cure among those with + urines; around 90% adherence despite ~50% +urines
SIMPLIFY ² : 103 persons who had injected drugs within 6 months treated sofosbuvir/velpatasvir	97% completed tx, 94% had SVR 12, drug use did not affect SVR 12
HERO study ³ : 755 persons who injected within 3 months treated with sofosbuvir/velpatasvir and randomized to patient navigation (PN) vs directly-observed treatment (DOT)	In both groups, >80% initiated treatment: of those, 92% had SVR 12 (no difference between arms); 74% adherence (non-adherence associated with no SVR)
PREVAIL study ⁴ : 145 PWID treated on-site at a methadone program with different DAA regimens via electronic blister packs	Overall, 96% had SVR 12 with average daily adherence 74% adherence; among those with ≥50% adherence, 99% achieved SVR 12 (<u>even with suboptimal adherence patients are cured!</u>)

1 Dore G, Annals Int Med 2016; 2 Grebely, Lancet Gastroenterol Hepat 2018; 3 Litwin, A Multisite Randomized Pragmatic Trial of Patient-Centered Models of Hepatitis C Treatment for People Who Inject Drugs: The HERO Study. Oral presentation at AASLD 2020, Nov 11-16

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Misconception #2 people who use drugs are likely to get re-infected

- Rate of reinfection among people who use drugs is low...

And substantially lower than rates of first infection

Hepatitis C treatment has been associated with reduced opioid injecting/sharing

- Reinfection can be prevented...

When people receive medications for opioid use disorder

When people use syringe service programs

Meta-analysis of rate of HCV reinfection

- Studied reinfection among 1) people who recently used drugs, and 2) those on opioid agonist treatment
- 36 studies with 6,311 person-years follow up

Population	# Studies	Person-years f/u	Rates of reinfection per 100 person-years
Injecting or non-injecting drug use	33	5,061	5.9 (95% CI 4.1-8.5)
Injecting drug use	31	4,648	6.2 (95% CI 4.3-9.0)
Opioid agonist treatment	25	2,507	3.8 (95% CI 2.5-5.8)



HCV treatment

- In most patients with hepatitis C, treatment is straight-forward and simple and can be done by PCPs with prescribing capacity (DO/MD/NP/PA)
 - In people with advanced liver disease or certain other conditions (hepatitis B co-infection, HIV, transplant, liver cancer), treatment is more complicated and should be done by or in consultation with specialists
-

Direct-Acting Antivirals for HCV

Typical treatment duration	8-12 weeks
Usual pill burden	1-3 pills taken once daily
Tolerability	Very well-tolerated overall Headache, fatigue, and nausea are relatively common but rarely interfere with treatment course
Effectiveness	>95% rate of sustained viral response at 12 weeks (SVR 12), now considered “cure” Comparable effectiveness in those with substance use
Examples (pan-genotypic)	Glecaprevir/pibrentasvir (Mavyret®) Sofosbuvir/velpatasvir (Epclusa®)

Screening for Hepatitis C Virus Infection



4 in 10

About 4 in 10 people with hepatitis C do not know they are infected.

4x

New hepatitis C cases are 4 times as high as they were 10 years ago.

20-39

Younger adults 20-39 years old have the highest rates of new hepatitis C cases.

- **New USPSTF recommendation to screen all asymptomatic adults age 18-79 for HCV: *Anti-HCV antibody followed by confirmatory PCR for viral detection***
- Those at high risk (e.g. past/current injection drug use) should be periodically rescreened: expert recommendation to rescreen annually

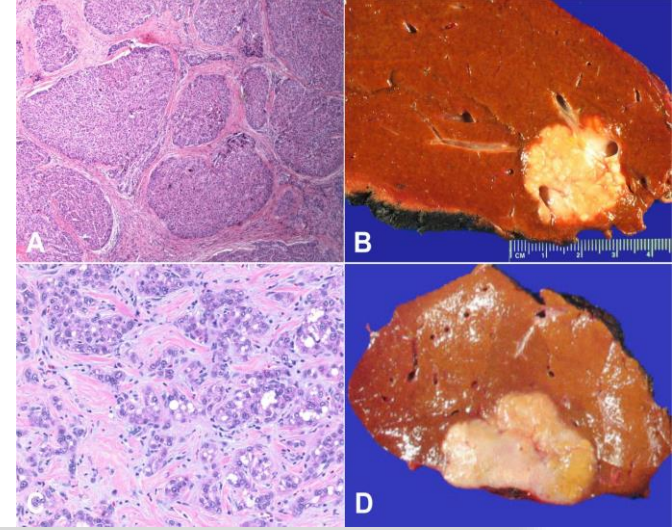
Pretreatment Assessment

Required	*Complete blood count (CBC), *Comprehensive metabolic panel (CMP), HCV RNA, HIV, HBsAg
Consider according to level of clinical concern for cirrhosis, based on... <ul style="list-style-type: none"> existing lab and imaging data (likely) duration of infection cumulative alcohol exposure signs/symptoms of cirrhosis 	International normalized ratio (INR) FibroTest/FibroSure®, ActiTest Transient elastography (<i>FibroScan</i>) Ultrasound
Treat as cirrhosis if any of the following	FIB-4 > 3.25 Platelet count < 150,000/mm ³ <i>FibroScan</i> > 12.5 kPa Liver nodularity and/or splenomegaly on imaging Prior liver biopsy showing cirrhosis

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \text{Result}$$

* Within 6 months of starting treatment

Screening Ultrasounds for HCC



Every 6
months for all
HBV patients

Every 6
months if HCV
and cirrhosis

When to Refer

Reasons to refer:

- Decompensated cirrhosis: ascites, jaundice, variceal hemorrhage, encephalopathy (Child's Class B or C)
- Hepatocellular carcinoma
- Post-transplant
- HBV and/or HIV
- *Prior treatment with DAAs

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			

Simplified HCV Treatment Algorithm: Patients *Without Cirrhosis*

Key Steps:

- Review medications, drug-drug interactions
 - Update labs as needed
 - Educate re: medication administration, adherence, and preventing reinfection

Treatment:

- Glecapresvir/pibrentasvir for 8 wks (3 pills daily with food), or
- Sofosbuvir/velpatasvir for 12 wks (1 pill daily)

Monitoring:

No lab monitoring required
Offer visits for support, assessment of symptoms

Patients With Compensated (Childs A) Cirrhosis

- There is also a simplified algorithm, **with some key differences:**

Check liver ultrasound to
exclude liver cancer
prior to treatment

Basic labs within 3 months

Check genotype*

Monitor for
decompensation**; refer to
specialist as needed

*If treating with sofosbuvir/velpatasvir. **Hepatic panel every 4 weeks; monitor for jaundice, ascites, encephalopathy.

Potential Drug Interactions

- Not all interactions require medication adjustment:
helpful to consult with pharmacist

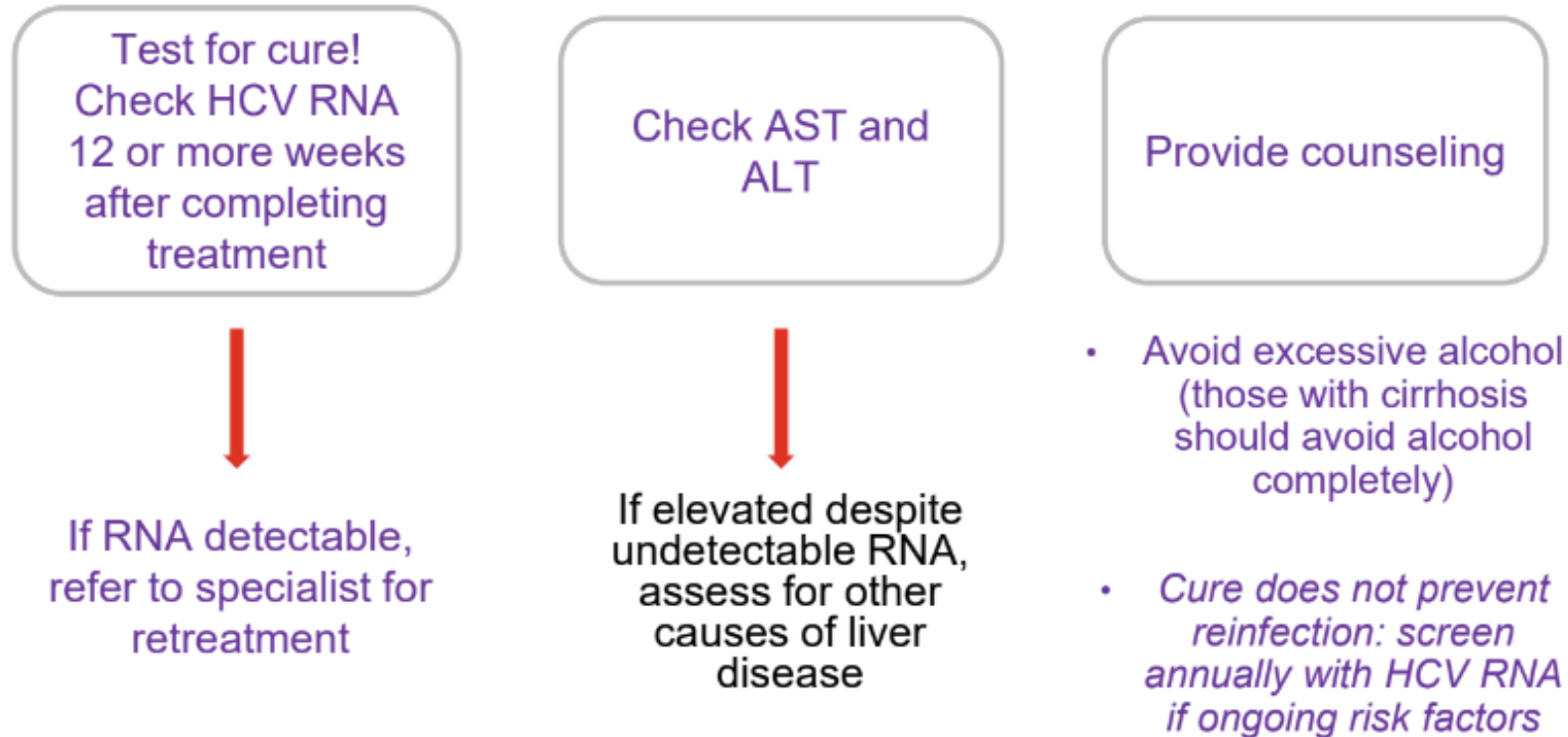
Glecaprevir/pibrentasvir (Mavyret®)

- Ethinyl estradiol containing medications (oral contraceptives)
- Statins
- DOACs (dabigatran) and antiarrhythmics (amiodarone, digoxin)
- Anticonvulsants (carbamazepine, phenytoin)
- Rifampin
- Antiretrovirals
- St. John's Wort

Sofosbuvir/velpatasvir (Epclusa®)

- Acid reducers (PPIs>H2B>antacids)
- Statins
- Antiarrhythmics (amiodarone, digoxin)
- Anticonvulsants (carbamazepine, phenytoin, phenobarbital)
- Antiretrovirals
- Rifampin
- St. John's Wort

Post-Treatment





Post treatment

- Great opportunity to address the Use Disorder! (Motivational interviewing)

Don't Forget Immunization!

- Recommend **hepatitis A and B** vaccination for people with OUD, whether or not they have HCV
 - Periodic outbreaks make this particularly important
- Those with cirrhosis, tobacco use, and/or heavy alcohol (among other conditions) should also receive **pneumococcal vaccination**

HCV take home points

Don't forget Q 6 months US if history of HBV or cirrhosis from any cause.

Screening for HCV via USPSTF recommendations in primary care

Immunize for HAV/HBV if not already immune

Take this great opportunity to treat the Use disorder. If OUD, MOUD!

There are FDA approved medications for OUD, AUD and Tobacco use disorder

If HCV/HBV co-infection will need to treat both. HCV in most cases is curative and HBV suppressive

Most cases of HCV can be treated by primary care!

HCV Treatment: Take-Home Points

- Simplified pathway w/ limited monitoring for most patients
- Adherence support helpful but DAAs are “forgiving” of imperfect adherence
- SVR 12 check is key
- Easy, fun, gratifying to cure people of an important disease
- Part of primary care, especially for people with OUD

References

- AASLD guidelines <https://www.hcvguidelines.org/>
- FBOP guidelines
- National Library of Medicine
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5479342/>
- IDSA <https://www.hcvguidelines.org/>



THANK YOU
for your
ATTENTION!