AETC AIDS Education & Training Center Program Mountain West

Hepatitis B and Hepatitis C in 2023 Diagnosis & Management

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Disclosures

No conflicts of interests or relationships to disclose.

Learning Objectives

- Describe the epidemiology, transmission, and natural history of hepatitis B and hepatitis C infection.
- Identify target populations for hepatitis B and hepatitis C screening and hepatitis B vaccination.
- Understand which patients with hepatitis B are likely to benefit from antiviral treatment and identify the recommended first line agents.
- Recognize patients at risk for hepatitis B reactivation and know when to initiate prophylactic treatment.
- Understand the pre-treatment evaluation for patients with hepatitis C and employ a simplified treatment algorithm to treat uncomplicated infection.

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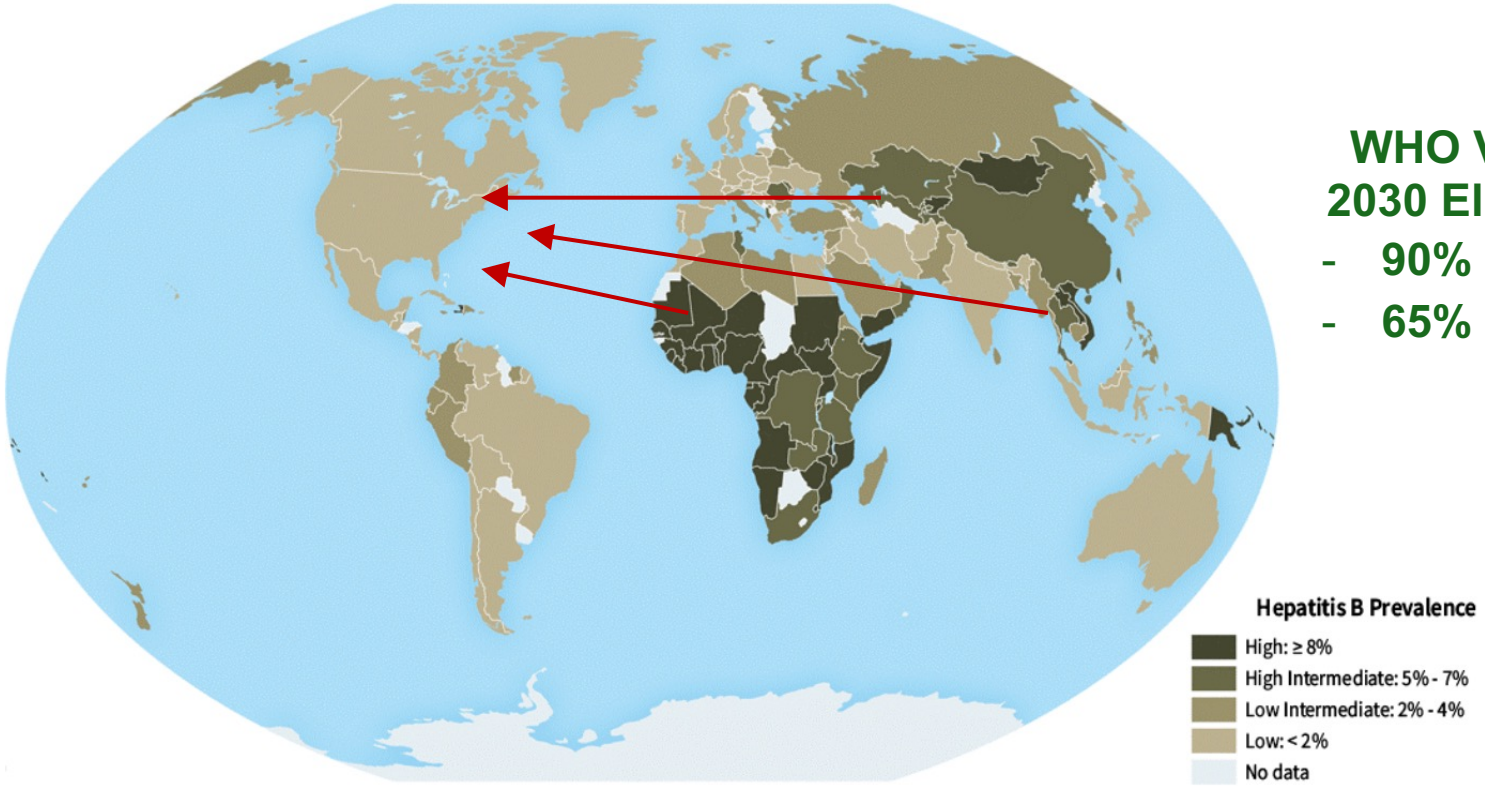
Hepatitis B

Global Prevalence of Hepatitis B Infection

296 million people living with chronic HBV globally



WHO Viral Hepatitis 2030 Elimination Goal

- **90% ↓ in new cases**
- **65% ↓ in mortality**

2 million people in the United States

World Health Organization. Hepatitis B: Key Facts. Geneva: WHO. June 2022.
Centers for Disease Control. CDC Yellow Book 2020.

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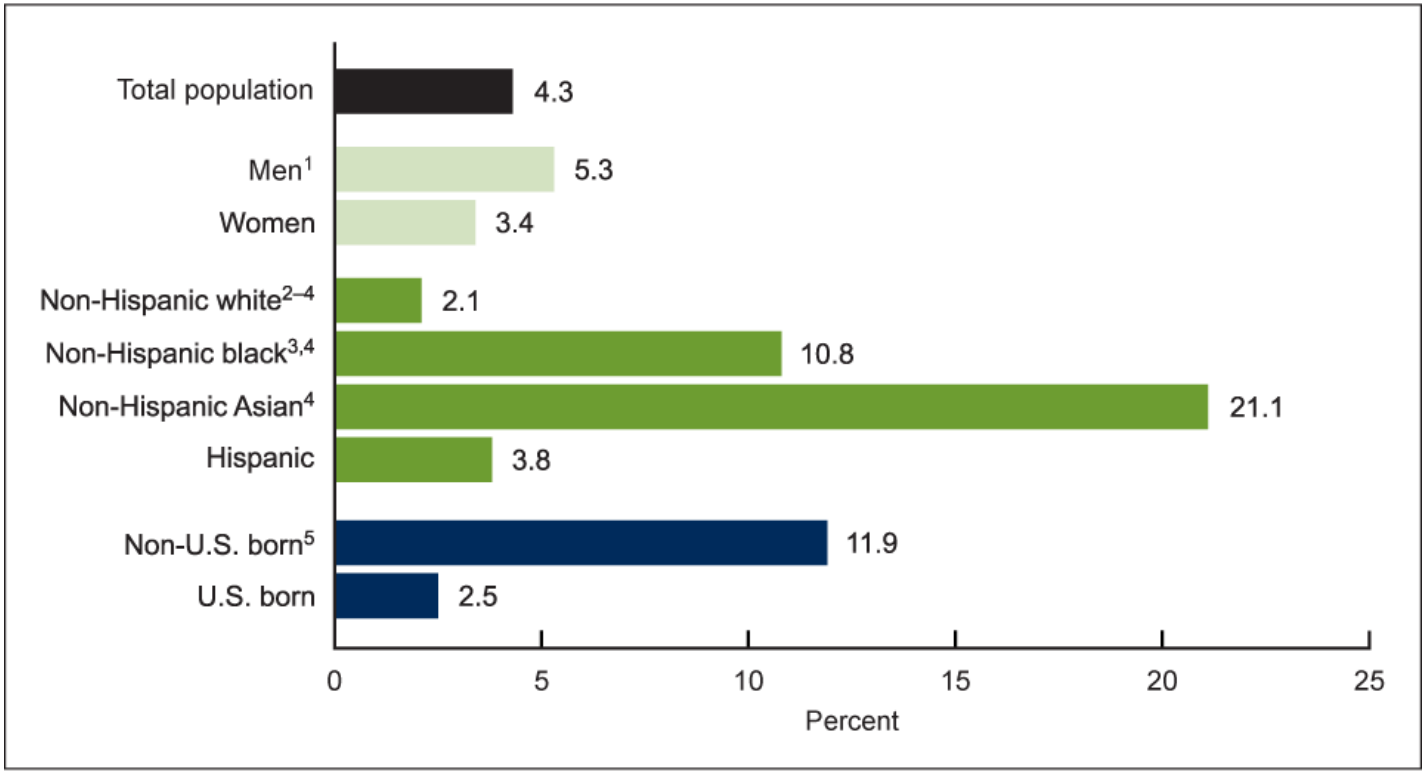
Hepatitis B Infection in the United States

Figure 1. Age-adjusted prevalence of past or present hepatitis B virus infection among adults aged 18 and over, by sex, race and Hispanic origin, and U.S. birth status: United States, 2015–2018



Kruszon-Moran et al. Prevalence and Trends in HepatitIS B Virus Infection in the U.S., 2015-2018. National Health and Nutrition Examination Survey. March 2020.

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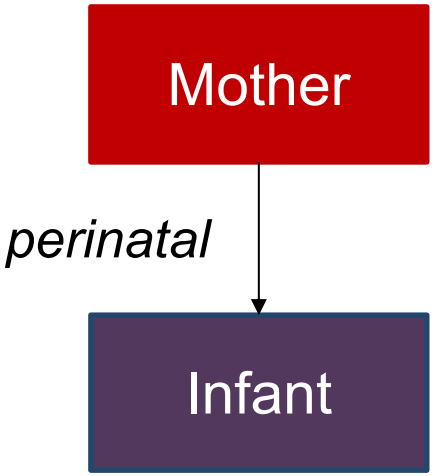
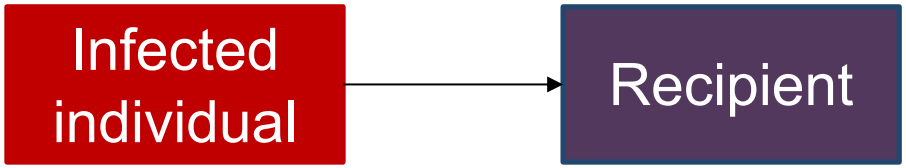
Transmission of Hepatitis B

Vertical Transmission



Common in areas of high prevalence

Horizontal Transmission



Sexual transmission

Injection drug use

Hemodialysis

Healthcare workers

Child to child

WHO Hepatitis B Fact Sheet. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. Accessed January 8,2023
Schweitzer, et al. *Lancet* 2015;386:1546-55.
Shihng et al. *Clin Infect Disease* 2020;70(12):2619-2627.

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Risk of Chronic Infection Varies by Age at Time of Transmission

Vertical Transmission	Childhood Infection	Adult Infection
~90%	20-50%	< 5%

Decreasing risk of progression to chronic infection

Increasing likelihood of symptomatic acute infection

Shiffman ML. Clinical Liver Disease 2010;14:75-92. Beasley et al. J Infect Dis 1982;146(2):198. Coursaget et al. J Med Virol. 1987;22(1):1. Tassopoulos et al. Gastroenterology. 1987;92(6):1844.

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High Burden of Disease Associated with Chronic Hepatitis B Infection

Cirrhosis: 30% of cirrhosis cases globally attributable to chronic hepatitis B infection.

Liver failure (decompensation): 15% incidence over 5 years among people with HBV-related cirrhosis[2]

Hepatocellular carcinoma (HCC): >50% of HCC cases globally attributable to chronic hepatitis B infection.[3]

Death: 820,000 deaths globally each year[4]

1. Perz JF et al. J Hepatol. 2006;45:529-538
2. Fattovich G, et al. J Hepatol. 2008;48:335-352.
3. Maucort-Boulch, et al. Int J Cancer. 2018;142(12):2471.
4. Centers for Disease for Control and Prevention. https://www.cdc.gov/hepatitis/hbv/index.htm. Accessed Jan 8, 2023.

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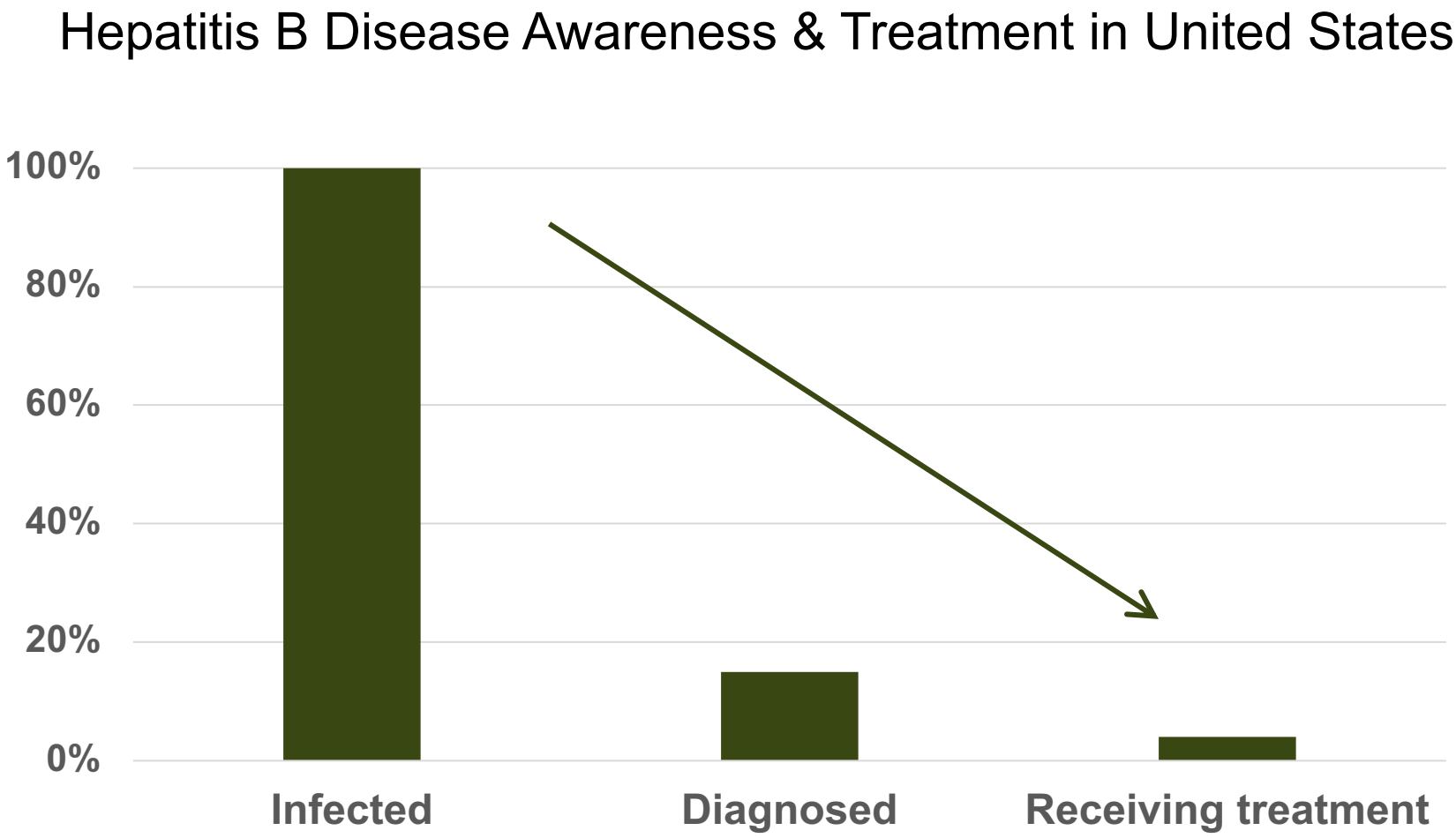
Underdiagnosis of HBV



Adapted from Ngyen et al. Hepatitis B Virus: Advances in Prevention, Diagnosis, and Therapy. Clin Microbiol Rev. 2020..

Screening for Hepatitis B Infection

HBsAg + anti-HBs + anti-HBc

USPSTF Recommendation: screen individuals at increased risk for hepatitis B infection

- Persons born in countries/regions with high prevalence (>2%), such as Asia, Africa, Pacific Islands
- US-born persons not vaccinated as infants whose parents were born in regions with very high prevalence (>8%)
- Persons living with HIV
- Persons who inject drugs (PWID)
- Men who have sex with men (MSM)
- Household contacts or sexual partners of persons with HBV infection

Hwang J, Lok AS. JAMA 2020;324(23):2380-2382

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Additional Groups to Test for HBV

- Persons in need of immunosuppressive therapy
- Persons with end stage renal disease
- Blood, organ, semen donors
- Pregnant persons
- Infants born to mothers with HBV infection
- Elevated liver tests

Hwang J, Lok AS. JAMA 2020;324(23):2380-2382

Currently Available Hepatitis B Vaccines

Vaccine	Year Approved	Type	Ages	Standard Adult Schedule
Recombivax-HB*	1986	Single antigen	All ages	3 doses at 0, 1, 6 months
Engerix-B*	1989	Single antigen	All ages	3 doses at 0, 1, 6 months
Twinrix (HAV-HBV)	2001	Combination	≥18yo	3 doses at 0, 1, 6 months
Hepislav	2017	Single antigen	≥18yo Not in pregnancy	2 doses at 0, 1 months
PreHevbrio	2021	Triple antigen	≥18yo Not in pregnancy	3 doses at 0, 1, 6 months

***Double dose recommended for patients with HIV infection**

Weng MK et al. MMWR Morb Mortal Wkly Rep. 2022;71(13):477. Epub 2022 Apr 1.

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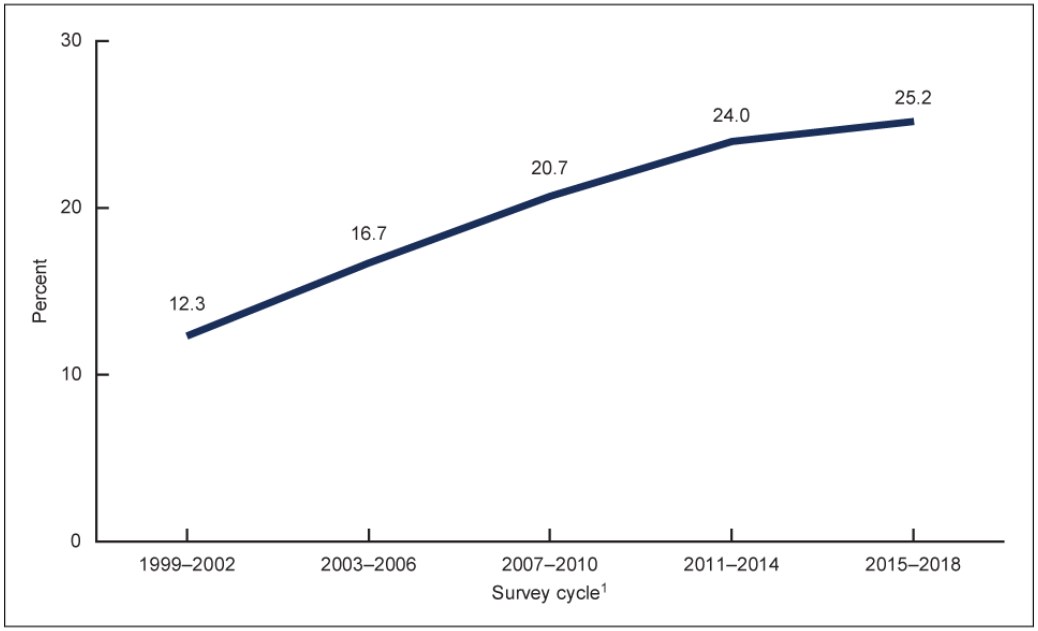
Vaccination is effective but underutilized among adults in the U.S.

- >90% immunity achieved among those < 40 years old[1,2]
- 91.4% U.S infants received HBV vaccination in 2016[3]
- Vaccination rates among U.S. adults are rising but remain low

Serologic evidence of HBV vaccination among U.S. adults



1.Averhoff et al. Am J Prev Med. 1998;15:1-8.
2.Jackson et al. Vaccine. 2018;36:668-674.
3.National Center for Health Statistics. Health, United States, [2010-2016]. Hyattsville, MD. [2021]. https://www.cdc.gov/nchs/hus/data-finder.htm.
Figure: Kruszon-Moran et al. National Health and Nutrition Examination Survey. March 2020.

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Recent Update to Hepatitis B Vaccination Recommendations

ACIP Recommendations - April 2022

All infants

Persons <19 years old

Adults 19-59 years old

Adults ≥ 60 years with risk factors:

- Sexual risk factors
- Injection drug use
- Healthcare and public safety personnel
- Hemodialysis
- International travelers to endemic regions
- History of Hepatitis C or HIV infection
- Incarceration

Weng MK et al. MMWR Morb Mortal Wkly Rep. 2022;71(13):477.

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Hepatitis B Serologies

HBsAg	Indicates active infection
Anti-HBs	Past infection or immunization
Anti-HBc	History of exposure to virus; IgM, IgG
HBeAg	Reflects high level of viremia & infectivity
Anti-HBe	↓ infectivity; favorable immune response
HBV DNA	Active infection

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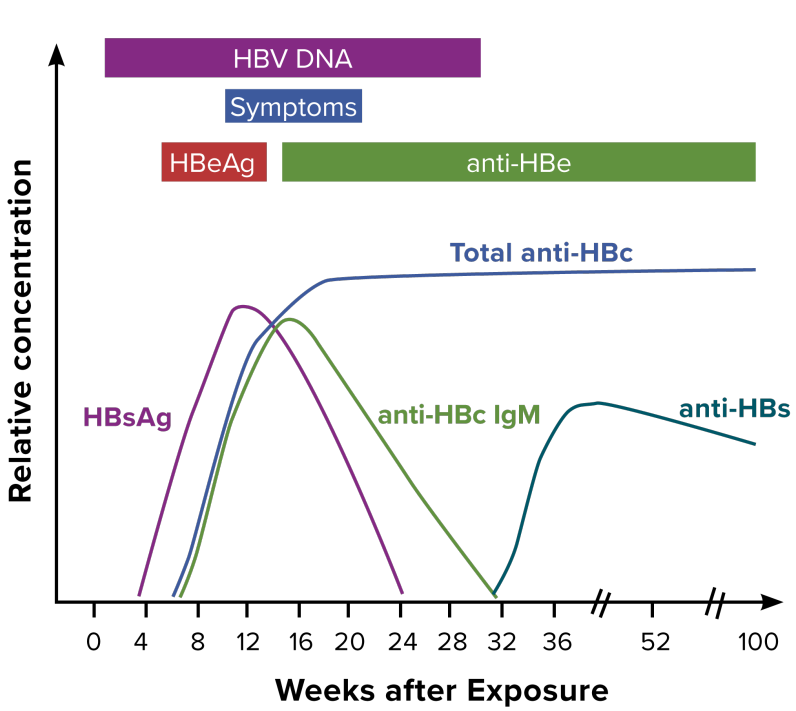
Typical Serologic Course of Hepatitis B

Acute Hepatitis B



Chronic Hepatitis B

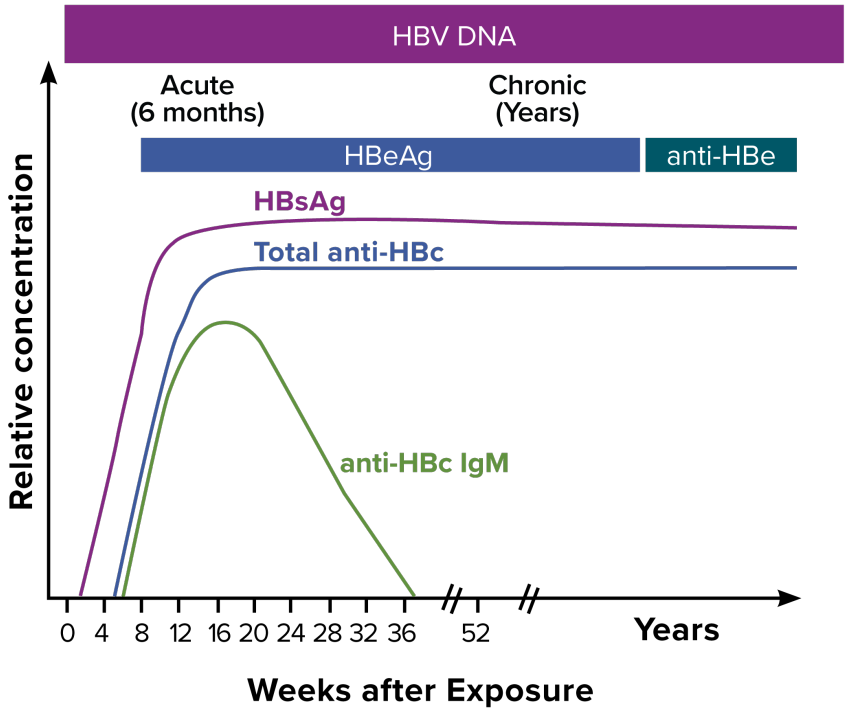


Figure obtained from https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm.

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Interpreting Hepatitis B Serologies

HBsAg	HBcAb	HBsAb	Interpretation
+	+	-	Chronic hepatitis B infection
-	+	+	Past infection, resolved
-	+	-	Past exposure with undetectable anti-HBs titers, prior chronic infection with loss of HBsAg, false positive
-	-	+	Vaccinated
-	-	-	Never infected, not immune

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Natural History of Chronic Hepatitis B Infection

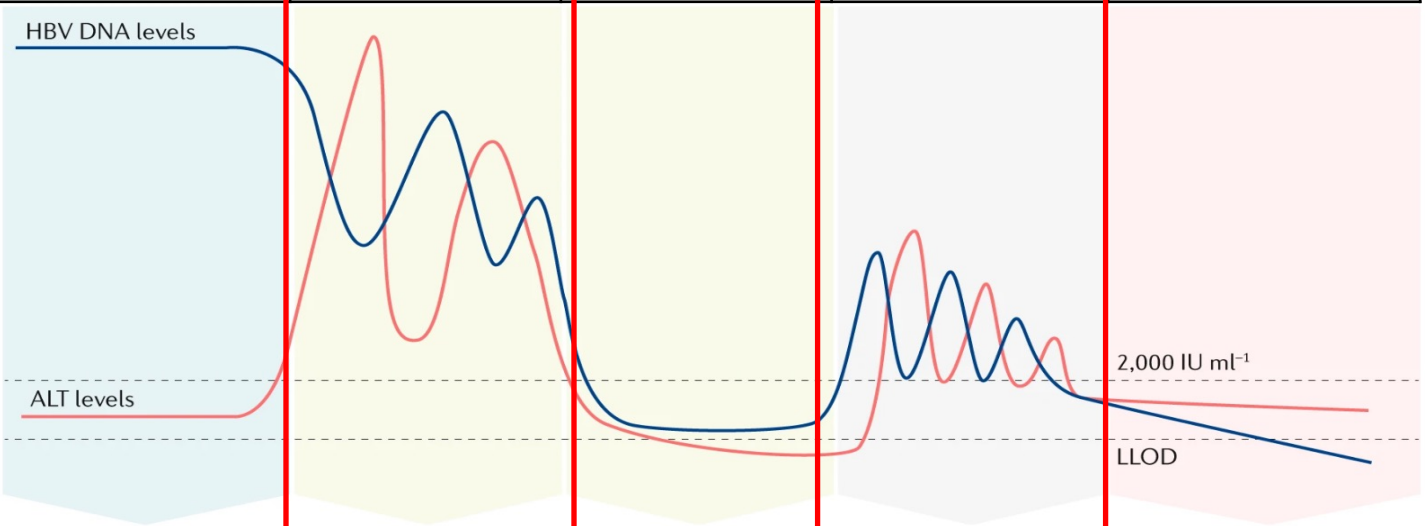
AASLD	Immune tolerant	Immune active HBeAg+ CHB	Inactive CHB	Immune active HBeAg- CHB	Resolved infection (HBsAg negative)
EASL	Chronic HBV Infection	Chronic hepatitis B	Chronic HBV Infection	Chronic hepatitis B	
Viral and liver inflammatory profile					
Serum HBsAg	+++++	++++	+	++	–
cccDNA	+++++	+++++	++	+++	+
Fibrosis	Minimal fibrosis	Variable degree of fibrosis (progressing)	Variable degree of fibrosis (progressing)	Moderate to severe fibrosis (resolving)	Variable fibrosis (sequelae of previous phases)
Liver inflammatory infiltrate	Absent	High	Absent/moderate	Moderate	Absent

Image: Fanning G et al. Nat Rev Drug Discov 2019;18(11):827-844.. Terrault et al. Hepatology 67(4):1560-1599
EASL Hepatitis B Clinical Practice Guielines. J Hepatol 2017;67:370-398

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HBV Treatment

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Audience question

Which of the following patients should be started on treatment for Hepatitis B?

A. 25 yo male with chronic HBV, eAg +, viral load 3 million, ALT 33

B. 43 yo male with acute HBV, eAg+, anti-HBc IgM+, viral load 800k, ALT 2,000, Tbili 2.4, INR 1.3

C. 27yo pregnant female, 26 weeks gestation, viral load 140k, ALT 23

D. 60yo female with chronic HBV, well-compensated cirrhosis with normal hepatic function, HBV viral load 900

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Hepatitis B Treatment Goals

Big Picture

- Improve survival by preventing cirrhosis, liver cancer, and need for liver transplant
- Prevent vertical transmission and viral reactivation

Specific Therapeutic Goals

- Undetectable serum HBV DNA (cannot eradicate HBV ccc DNA)
- Normal ALT
- Improvement in liver histology
- HBeAg clearance
- HBsAg loss (functional cure)

EASL Hepatitis B Clinical Practice Guielines. J Hepatol 2017;67:370-398

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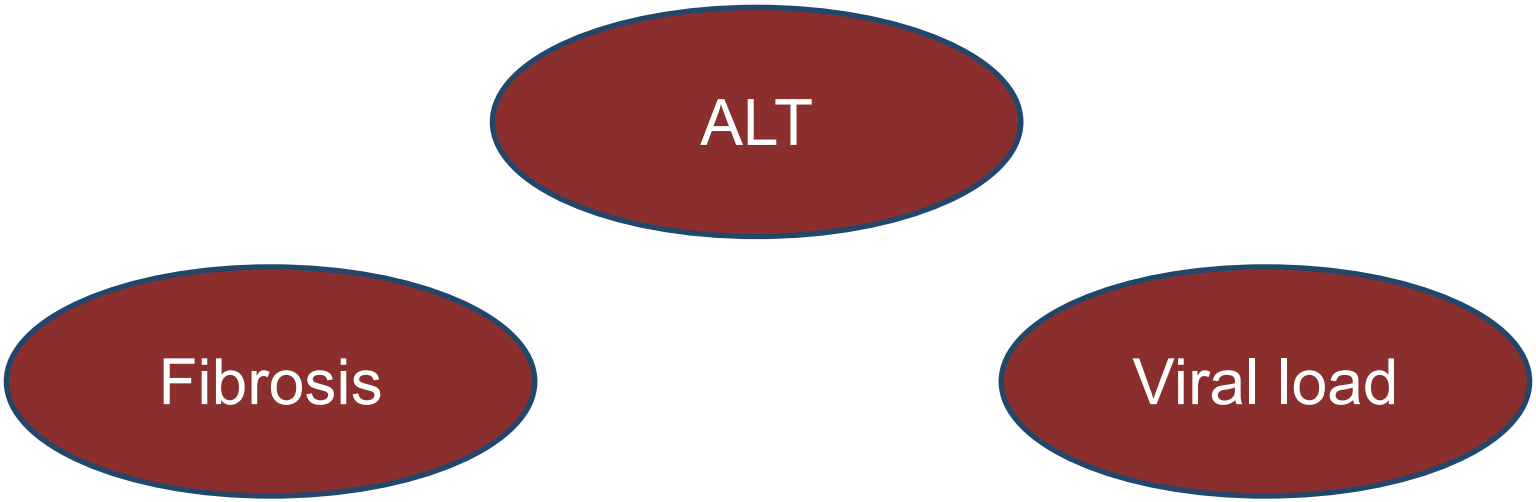
Determining Who to Treat: 3 Key Factors



Target patients at risk for liver-related complications

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Who to Treat?

Should treat:

1. Cirrhosis – regardless of ALT
2. Elevated ALT + elevated HBV viral load (*immune active disease*)

   ALT ≥ 2x ULN (35 males, 25 females)

   HBV DNA ≥2,000 (eAg neg), ≥20,000 (eAg pos)

Consider treatment:

1. Significant fibrosis or inflammation but viral load and/or ALT below thresholds
2. Age ≥40 + elevated viral load

Patients not on treatment should undergo routine lab monitoring at least every 6 months with HBV DNA and hepatic function panel

Terrault et al. Hepatology 67(4):1560-1599. EASL Hepatitis B Clinical Practice Guielines. J Hepatol 2017;67:370-398. Sarin SK et al. Hepatol Int. 2016;10:1-98.

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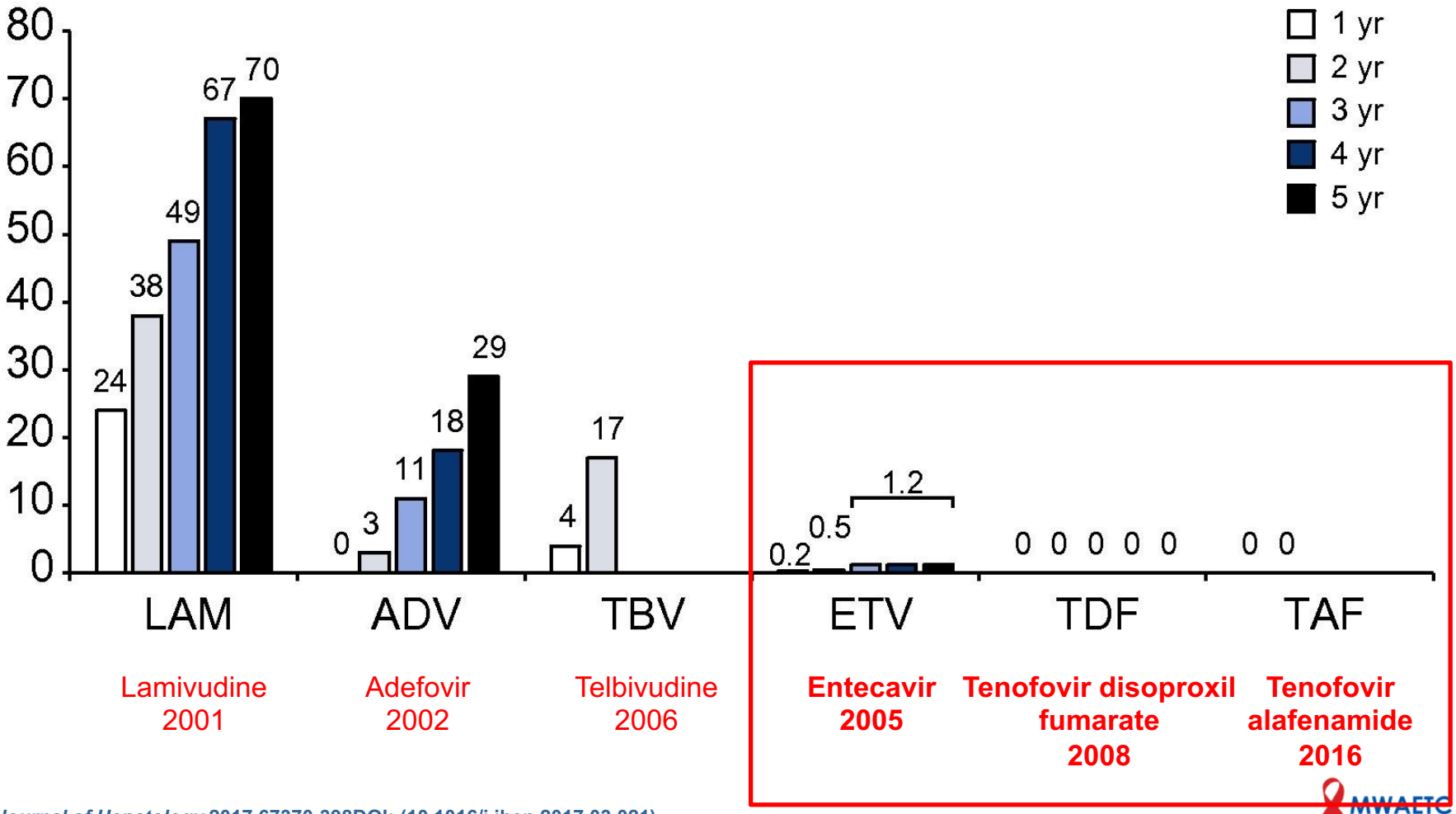
HBV Treatment: Nucleoside Analogs

Cumulative incidence of HBV resistance for nucleoside analogs in nucleoside-naïve patients with chronic hepatitis B.



Journal of Hepatology 2017 67370-398DOI: (10.1016/j.jhep.2017.03.021)

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HBV Treatment: First Line Treatments

Medication	Dose	Considerations
Entecavir	0.5-1mg PO daily	Increased risk of resistance if prior history of lamivudine treatment
Tenofovir disoproxil fumarate	300mg PO daily	Risk of decreased GFR, decreased bone density Preferred agent in pregnancy
Tenofovir alafenamide	25mg PO daily	Appropriate for use in patients with CKD, osteoporosis, age ≥60
Peginterferon alfa-2a	180mcg SQ weekly 48 weeks	Poorly tolerated. Flu-like symptoms, myelosuppression, neuropsychiatric side effects Avoid in decompensated cirrhosis.

Terrault et al. Hepatology 2018;76(4): 1560-1594

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HBsAg loss is rare with nucleoside analog treatment

HBeAg+ patients: results at 6 months after initial 48 or 52 weeks of therapy

	PEG-IFN	ETV	TDF	TAF
HBV DNA <60-80IU/mL	7-14%	67%	76%	64%
ALT normalization	32-41%	68%	68%	72%
Anti-HBe seroconversion	29-32%	21%	21%	10%
HBsAg loss	3-7%	2%	3%	1%

HBeAg- patients: results at 6 months after initial 48 or 52 weeks of therapy

	PEG-IFN	ETV	TDF	TAF
HBV DNA <60-80IU/mL	19%	90%	93%	94%
ALT normalization	59%	78%	76%	83%
HBsAg loss	4%	0%	0%	0%

Key point: *most patients started on nucleoside analogs will require lifelong treatment*

EASL Hepatitis B Clinical Practice Guidelines. J Hepatol 2017;67:370-398

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Nucleoside Analogs: Therapeutic Endpoints

HBeAg (+)	HBeAg (-)	Cirrhosis
HBsAg loss *or* HBeAg loss + ≥1 year of consolidation therapy	HBsAg loss	Indefinite therapy

If stopping therapy, <u>need to monitor labs</u> (ALT, HBV VL) every 3 months to assess for flare

Papatheodoridis et al. Hepatology 2016;63:1481-1492.

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Hepatocellular Carcinoma Screening

Liver ultrasound +/- AFP every 6 months

AASLD

Cirrhosis
Asian or black males > 40 yo
Asian females > 50 yo
Family history of HCC
Hepatitis D coinfection

EASL

Cirrhosis
Long term NA therapy
Moderate or high-risk HCC scores

Terrault et al. Hepatology 67(4):1560-1599
EASL Hepatitis B Clinical Practice Guielines. J Hepatol 2017;67:370-398

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Acute Hepatitis B

- >95% of patients will spontaneously clear infection
  - → Do not require treatment

- Consider treatment for those with severe acute hepatitis B → entecavir, TDF, or TAF
  - Tbili > 3, INR >1.5, ascites, encephalopathy
  - Protracted course (jaundice > 4 weeks)

- Patients with severe acute hepatitis B with signs of acute liver failure should be referred for liver transplant evaluation

EASL Hepatitis B Clinical Practice Guielines. J Hepatol 2017;67:370-398

HBV & HIV Co-Infection: Treatment Recommendations

Increased risk liver-related morbidity and mortality in patients with HIV and HBV coinfection

- All patients with HIV/HBV co-infection should receive concomitant treatment for HBV, regardless of HBV DNA, ALT, or degree of fibrosis
- Antiretroviral therapy (ARVT) should include 2 drugs that are active against HBV → TDF or TAF + lamivudine or emtricitabine
- Entecavir should only be used with a fully suppressive ARVT regimen due to risk of HIV resistance mutations
- Counsel patients on risk of HBV flare if therapy stopped or interrupted [(including those with chronic HBV on Pre-Exposure Prophylaxis (PrEP)]

Thio CL et al. Lancet 2002;360:1921-6.
World Health Organization. HBV-HIV Coinfection. June 2022. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b
Terrault et al. Hepatology 2018;76(4): 1560-1594

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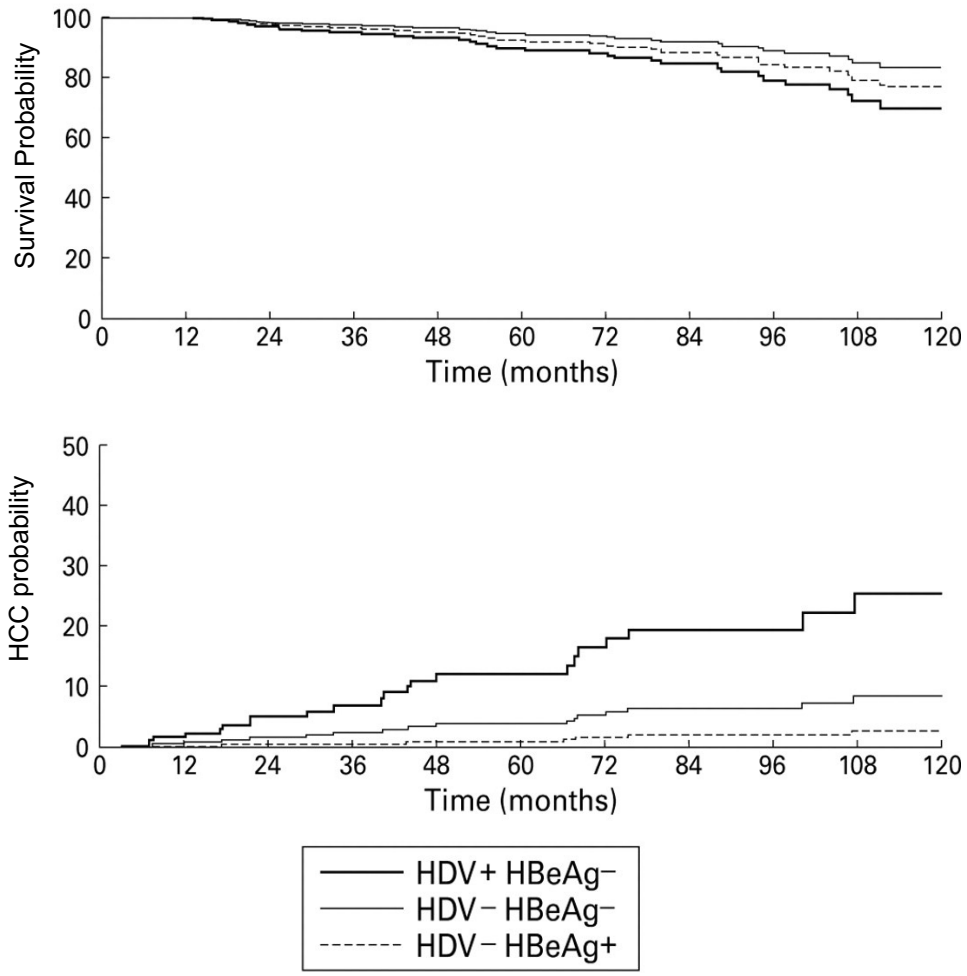
Hepatitis D Infection



↑ **Decompensation**

↑ **HCC**

↓ **Survival**

G Fattovich et al. Gut 2000;46:420-426

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Hepatitis D Infection: Screening & Management

Screening

HDV Ab → **HDV DNA**

TABLE 7. HBsAg-Positive Persons at High Risk of HDV Infection Who Should Be Screened

- Persons born in regions with reported high HDV endemicity*
  - Africa (West Africa, horn of Africa)
  - Asia (Central and Northern Asia, Vietnam, Mongolia, Pakistan, Japan, Taiwan)
  - Pacific Islands (Kiribati, Nauru)
  - Middle East (all countries)
  - Eastern Europe (Eastern Mediterranean regions, Turkey)
  - South America (Amazonian basin)
  - Other (Greenland)
- Persons who have ever injected drugs
- Men who have sex with men
- Individuals infected with HCV or HIV
- Persons with multiple sexual partners or any history of sexually transmitted disease
- Individuals with elevated ALT or AST with low or undetectable HBV DNA

Treatment

PEG-IFN alpha
≥48 weeks*

↓

Low rates of sustained response

Terrault et al. AASLD 2018 Hepatitis B Guidance. *Hepatology* 2018.

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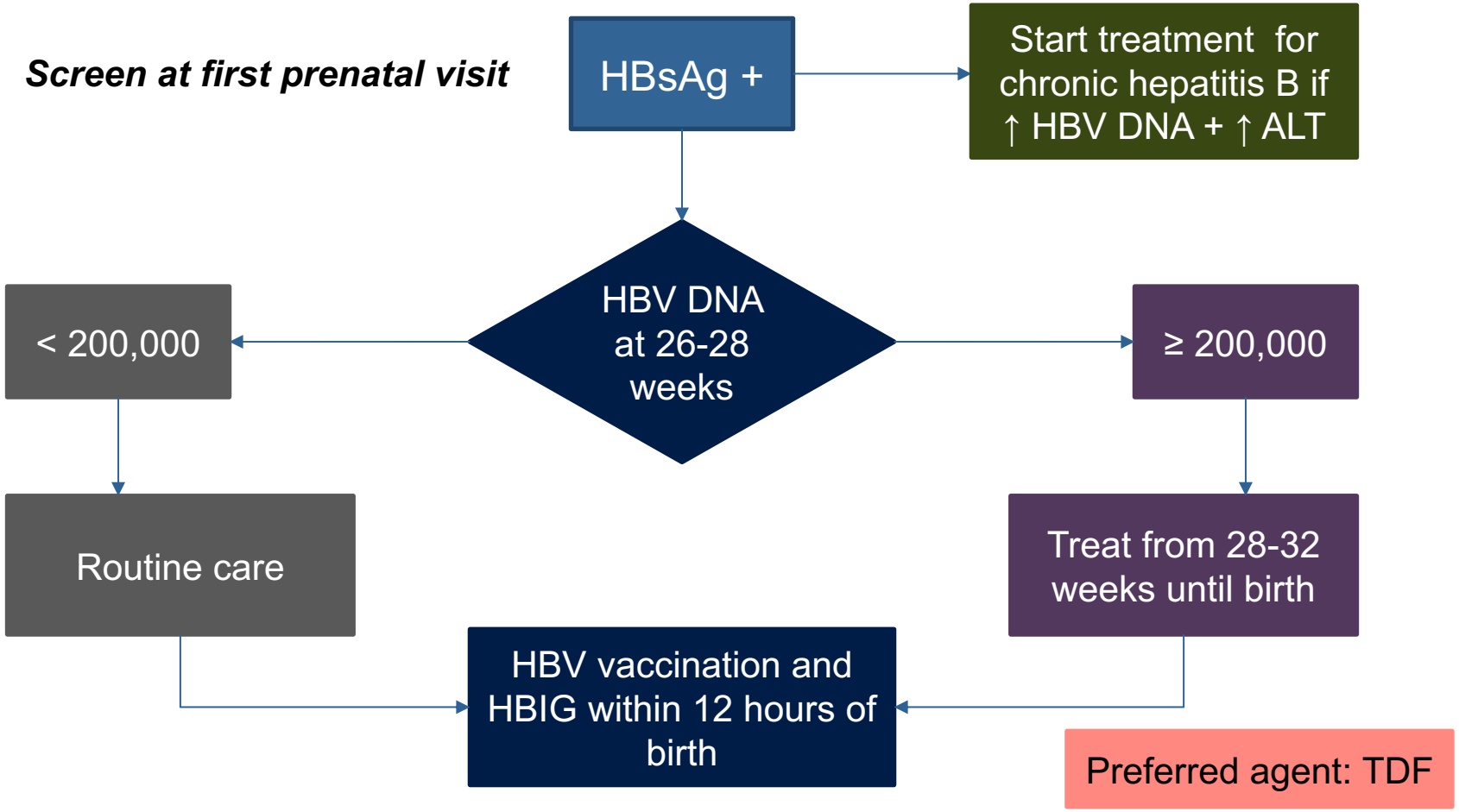
Hepatitis B Treatment in Pregnancy



Breastfeeding is not contraindicated in mothers with chronic HBV, on or off therapy

Dionne-Odom J et al. Am J Obstet Gynecol 2016;214:6-14.

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Hepatitis B Reactivation

Loss of immune control of inactive or resolved hepatitis B infection.

- Abrupt increase in viral replication → liver damage resulting from immune response
- May occur in patients with chronic hepatitis B (sAg+) or resolved hepatitis B (sAg-, cAb+)
- Severity ranging from subclinical to acute liver failure and death
- Patients should be tested for hepatitis B prior to undergoing immune suppressive therapy → HBsAg, anti-HBs, anti-HBc

Myint et al. Clinical Liver Disease 2020;15(4):162-167.

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HBV Reactivation: Risk Stratification

Reactivation Risk	HBsAg (+)	HBsAg (-) HBcAb (+)
High >10%	B cell depleting agents SCT High dose corticosteroids Anthracyclines Anti-TNF agents	B cell depleting agents SCT
Moderate 1-10%	Systemic chemotherapy Cytokine inhibitors Tyrosine kinase inhibitors Moderate dose corticosteroids	High dose corticosteroids Anthracyclines Anti-TNF agents Systemic chemotherapy Cytokine inhibitors Tyrosine kinase inhibitors Moderate dose corticosteroids
Low <1%	Antimetabolites Short term low dose (<10mg daily) steroids Intra-articular steroid injections	Antimetabolites Short term low dose (<10mg daily) steroids

Reddy et al. Gastroenterology 2015;148(1):215-9.
Myint et al. Clinical Liver Disease 2020;15(4):162-167.

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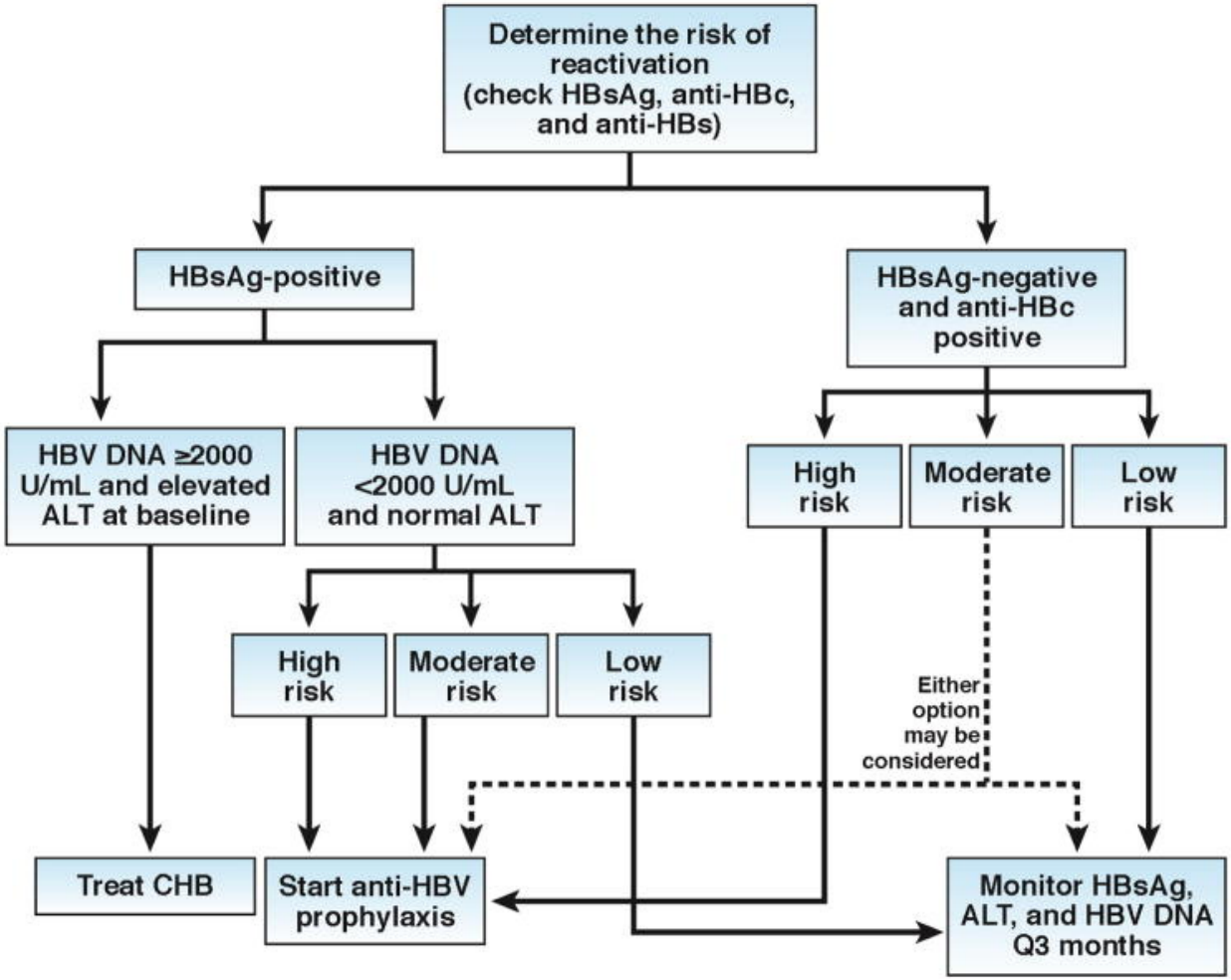
Preventing HBV Reactivation



Continue prophylaxis for 6 months after immunosuppression (12 months if rituximab)

Loomba R, Liang TJ. Hepatitis B Reactivation Associated with Immune Suppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions. Gastroenterology. 2017

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Hepatitis C

The Scope of Hepatitis C Infection

- Estimated 58 million people living with chronic hepatitis C infection worldwide[1]
- Estimated 2.4 million people living with hepatitis C in the United States between 2013-2016[2]
- Incidence of new HCV infection increasing in the United States over the last decade[3]

[1]WHO Fact Sheet. Hepatitis C. Updated June 24, 2022.
[2]Hofmeister et al. Estimating prevalence of hepatitis C Virus Infection in the United States, 2013-2016. Hepatology. 2019;69:1020–31
[3]Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2020.

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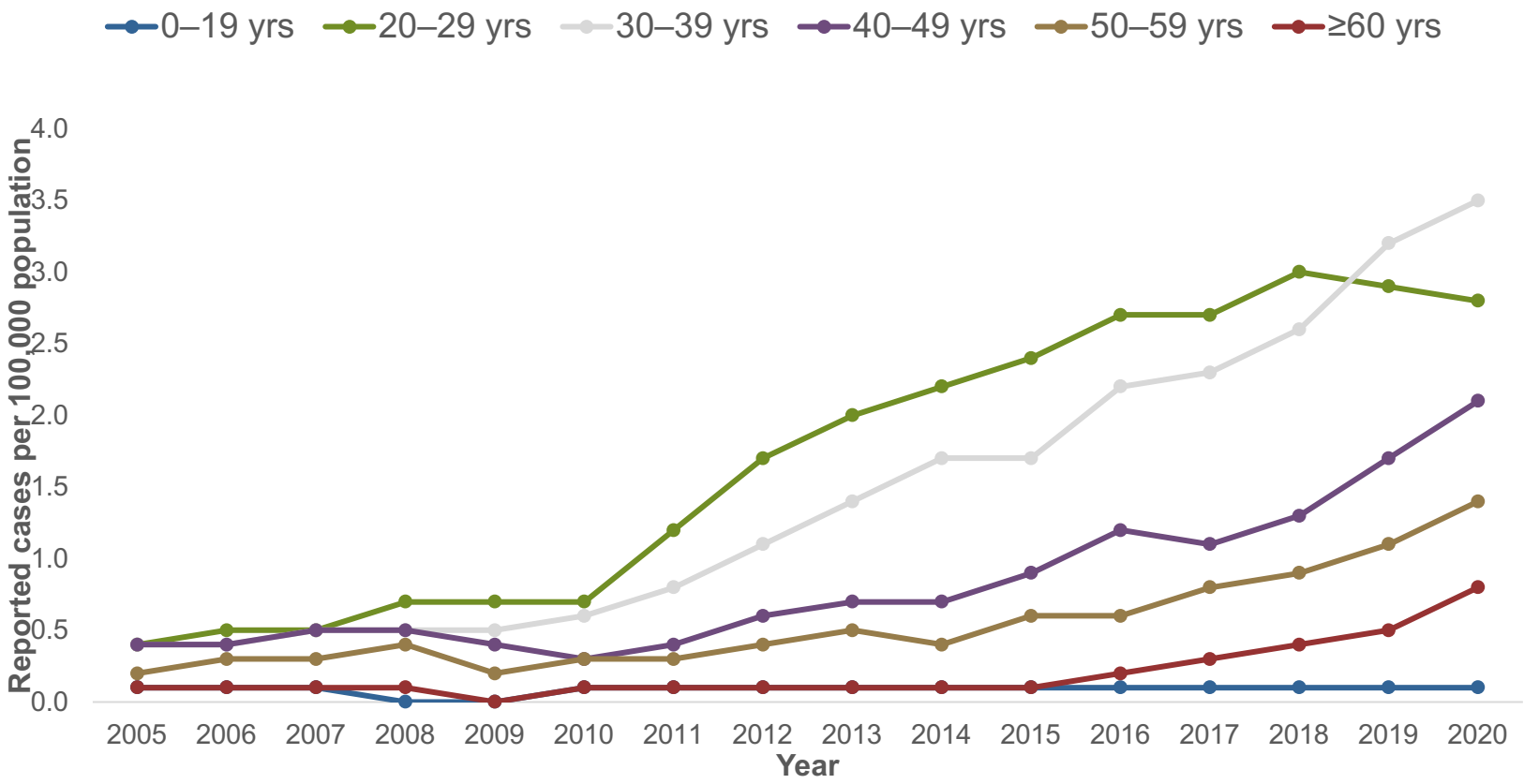
Rising incidence of HCV with disproportionate increases among young people

Incidence of reported cases of acute HCV infection. United States, 2005–2020



Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2020. https://www.cdc.gov/hepatitis/statistics/2020surveillance/index.htm. Published September 2022.

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Hepatitis C: Routes of Transmission

Injection drug use

Accounts for >60% of new cases of HCV infection in U.S.

Perinatal transmission

~5.8% risk among mothers with HCV

Sexual transmission (↑ risk among MSM with HIV)

Sharing contaminated personal items

Needle exposure (healthcare, tattooing)

Blood, blood product transfusion (rare since 1992)

Schillie et al. MMWR Recomm Rep 2020.
Williams IT, Bell BP, Kuhnert W, Alter MJ. Incidence and transmission patterns of acute hepatitis C in the United States, 1982-2006. Arch Intern Med. 2011;171:242-8.
Degenhardt et al. Lancet Global Health 2017;5(12):E1192-1207.

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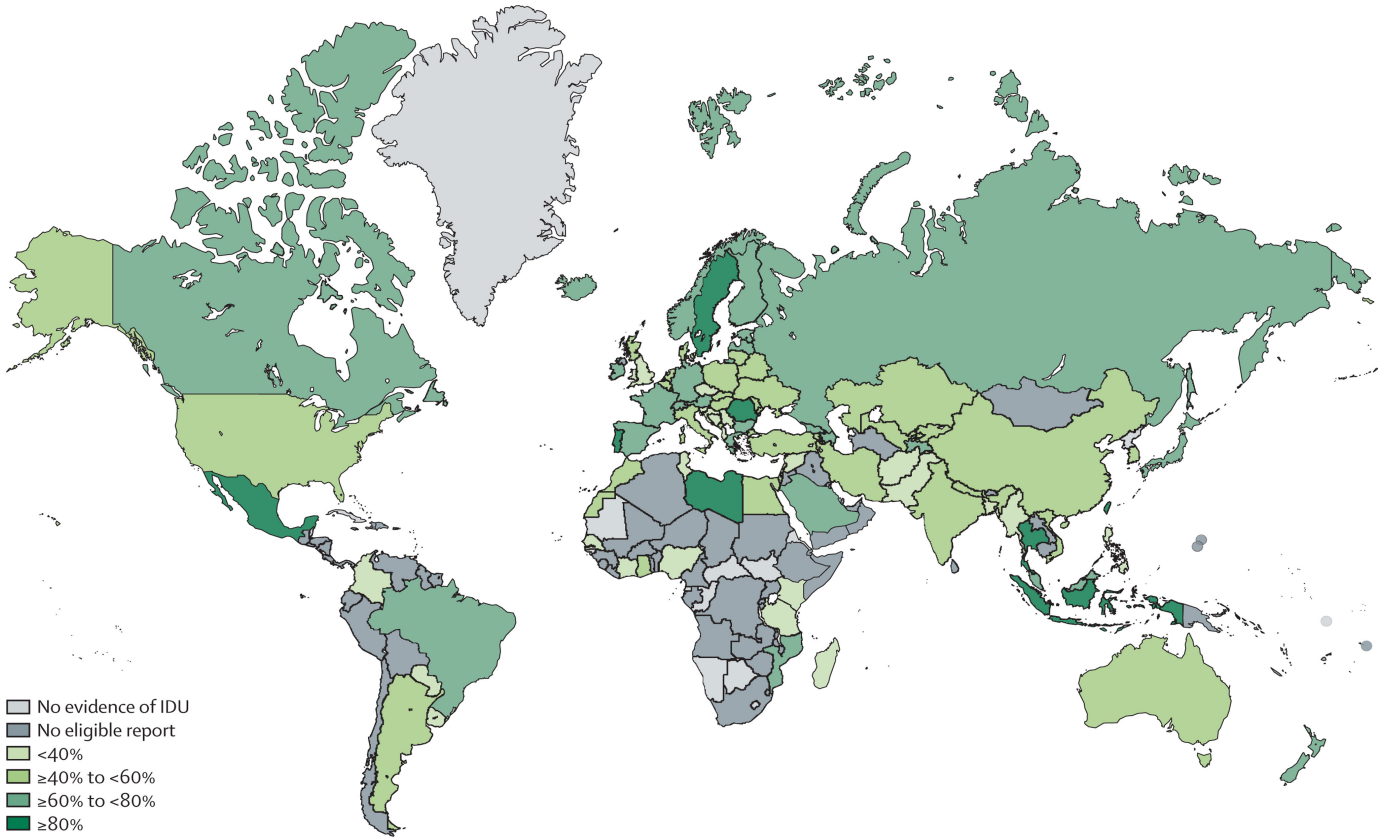
HCV Prevalence Among PWID

55.2% prevalence of anti-HCV Ab among PWID in North America



[1]Degenhardt et al. Lancet Global Health 2017;5(12):E1192-1207.

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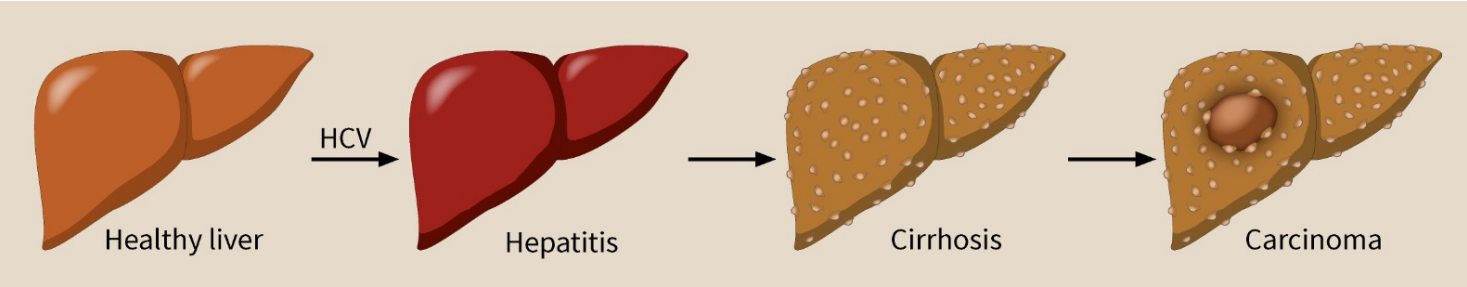
Hepatitis C: Natural History

Chronic infection in 60-80% of cases

Cirrhosis takes decades to develop

↑ risk with:
Chronic alcohol use
NAFLD
HIV or HBV co-infection



HCV RNA (+) within 2-3 weeks of exposure

HCV antibody (+) 2-3 months after exposure → *Persists lifelong*

Illustration: www.hegasy.de (open source)

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HCV Screening Strategy in 2023

Universal screening + **Risk-based screening**

Population	Recommendation	Grade
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

USPSTF

RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older.	I, B
Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy.	I, B

AASLD/IDSA

AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care. Chou R, Dana T, Fu R, et al. JAMA. 2020; 323(13):1318.

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Risk-Based Screening for HCV

1. **One time screening** for persons <18yo with known exposures or at high risk for infection
2. **Annual testing** for:
    1. All persons who inject drugs
    2. MSM who are living with HIV and engaging in unprotected sex
    3. MSM taking PrEP
3. **Periodic repeat testing** for people at increased risk for infection

AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.

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Risk Factors for HCV Infection

Risk Activities

- Injection drug use
- Intranasal drug use
- Use of glass cocaine pipes
- Unprotected sex among MSM
- “Chemsex”

Risk Exposures

- History of incarceration
- Long term hemodialysis
- Needlestick, sharps or mucosal exposure
- Children born to mothers infected with HCV
- Blood transfusion or organ transplant before 1992

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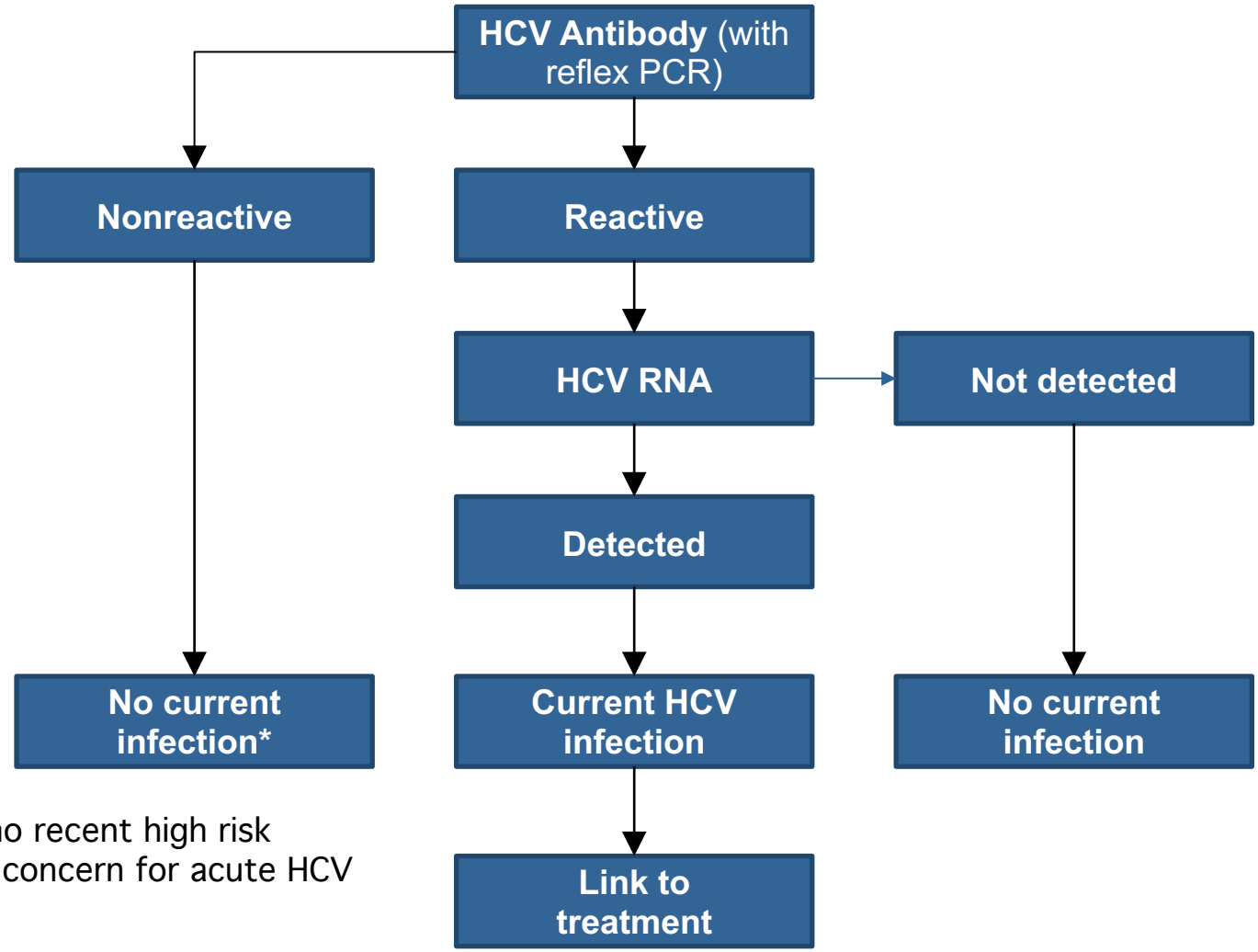
How to Screen for HCV?



*Assuming no recent high risk exposure or concern for acute HCV

Adapted from AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.

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Counseling Patients with Hepatitis C Infection

- Alcohol abstinence
- HAV, HBV vaccination

Prevent disease progression

- Harm reduction treatment for substance use disorders
  - Medication for opioid use disorder
  - Single use syringes, no sharing needles
- Cover wounds, avoid sharing toothbrushes/razors
- Patients with multiple sexual partners and those with HIV should use barrier protection.
- Patients with HCV infection should not donate blood
- Treatment of HCV recommended prior to pregnancy

Prevent transmission

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Hepatitis C Treatment

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Audience Question

A 47 year old man with a history of opioid use disorder and HCV-related cirrhosis (CTP B) presents to your clinic to discuss hepatitis C treatment. He continues to use intravenous drugs. His MELD-Na score is 17. Labs show Na 136, Cr 1.2, AST 64, ALT 80, Tbili 2.1, INR 1.6, albumin 3.4, HCV RNA 4 million, HCV genotype 2. He has minimal ascites, no hepatic encephalopathy. What is the most appropriate course of action?

A. No treatment due to active drug use

B. Ledipasvir/sofosbuvir/ribavirin x 12 weeks

C. Glecaprevir/pibrentasvir x 24 weeks

D. Refer for liver transplant

E. Sofosbuvir/velpatasvir x 24 weeks

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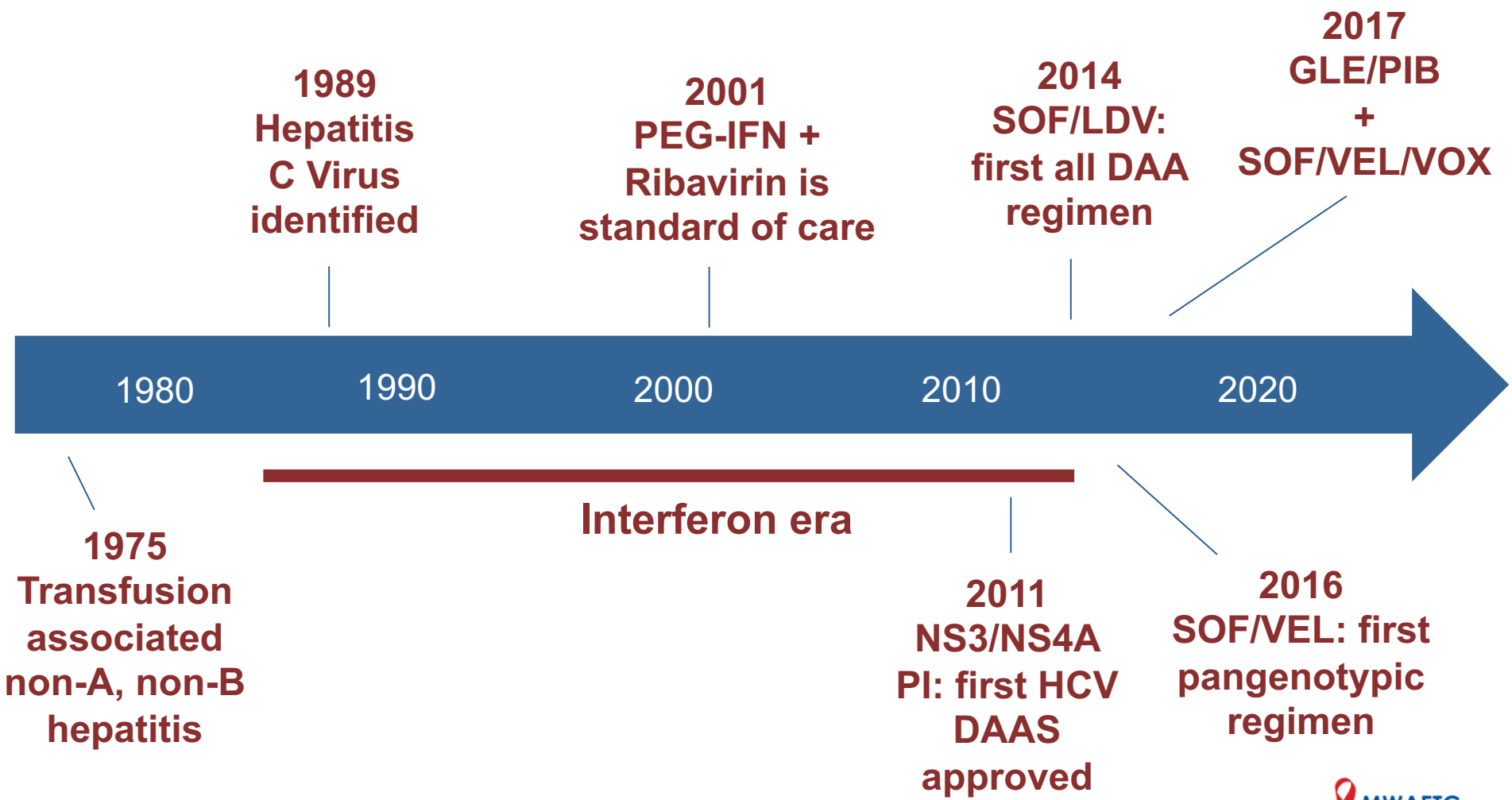
The Direct Acting Antiviral Revolution



Basyte-Bavevice V, Kupcinkas J. Dig Dis 2020;38:137-142.

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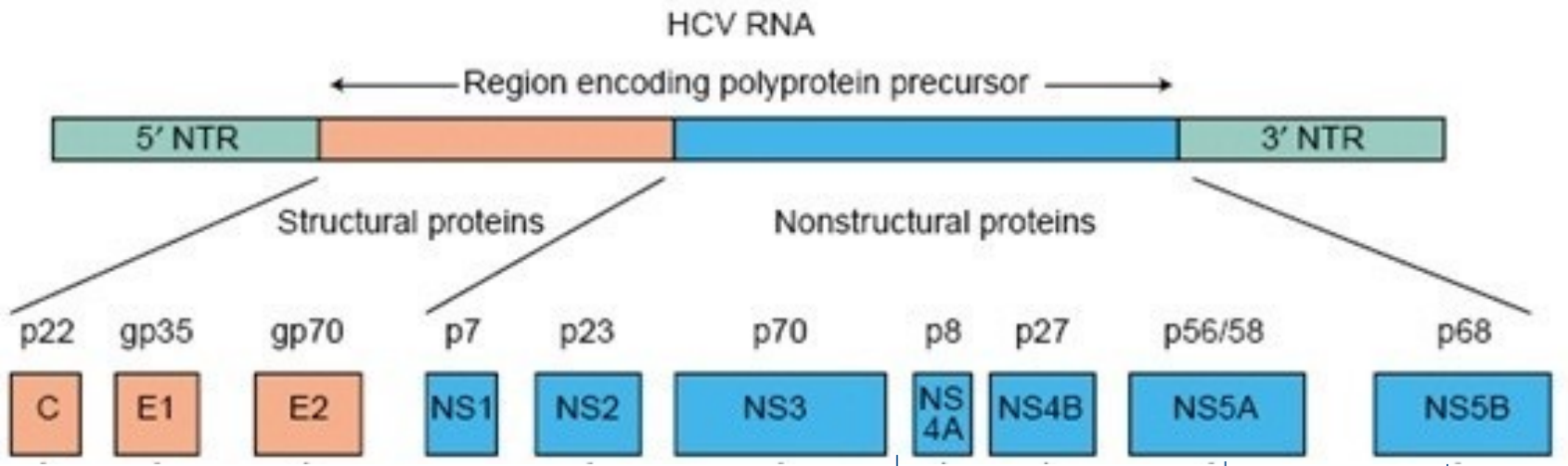
Combination Direct-Acting Antiviral Therapies Target Multiple HCV Proteins



Currently approved DAAs

NS3/4A Protease Inhibitors	NS5A Replication Complex Inhibitors	NS5B Nucleotide Inhibitors
Glecaprevir	Ledipasvir	Sofosbuvir
Grazoprevir	Velpatasvir	
Voxilaprevir	Pibrentasvir	
	Elbasvir	

Adapted from Ashfaq UA, et al. Virol J 2011;8(161)

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Who to Treat?

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

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Evaluation Before HCV Treatment

Laboratory

- CBC
- Hepatic function panel
- INR
- eGFR
- HCV RNA
- +/- HCV genotype
- HBsAg, anti-HBs, anti-HBc
- HIV
- Pregnancy test

Fibrosis staging

- FIB-4, APRI
- Transient elastography (Fibroscan)
- Liver biopsy
- Clinical evidence of cirrhosis

Drug-drug interactions

- Proton pump inhibitors
- Statins
- Anti-epileptics
- ARVT

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First Line DAA Regimens for HCV Treatment

	No cirrhosis		Compensated cirrhosis	
Genotype	**Regimen**	**Duration**	**Regimen**	**Duration**
1	GLE/PIB SOF/VEL LED/SOF EBR/GZR (1b)	8 weeks 12 weeks 8-12 weeks 12 weeks	GLE/PIB SOF/VEL LED/SOF EBR/GZR	8 weeks 12 weeks 12 weeks 12 weeks
2, 3*	GLE/PIB SOF/VEL	8 weeks 12 weeks	GLE/PIB SOF/VEL	8 weeks 12 weeks
4	GLE/PIB SOF/VEL LED/SOF EBR/GZR	8 weeks 12 weeks 12 weeks 12 weeks	GLE/PIB SOF/VEL LED/SOF EBR/GZR	8 weeks 12 weeks 12 weeks 12 weeks
5, 6	GLE/PIB SOF/VEL LED/SOF	8 weeks 12 weeks 12 weeks	GLE/PIB SOF/VEL LED/SOF	8 weeks 12 weeks 12 weeks

*If baseline NS5A RAS Y93H → SOF/VEL/RBV or SOF/VEL/VOX x 12 weeks

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AASLD/IDSA Simplified Hepatitis C Treatment

Who qualifies?

Adults with chronic HCV

+

No prior treatment

+

No cirrhosis *or* compensated cirrhosis

Who does not qualify?

Prior HCV treatment

Decompensated cirrhosis

HIV or HBV infection

ESRD + cirrhosis

Pregnant patients

Hepatocellular carcinoma

Prior liver transplant

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AASLD/IDSA Simplified Hepatitis C Treatment

Patients without cirrhosis

All genotypes

Glecaprevir 300mg/pibrentasvir 120mg (Mavyret) 8 weeks	Sofosbuvir 400mg /velpatasvir 100mg (Epclusa) 12 weeks

AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.

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AASLD/IDSA Simplified Hepatitis C Treatment

Patients with compensated cirrhosis

All genotypes

Glecaprevir 300mg/pibrentasvir 120mg (Mavyret)

8 weeks

*Genotypes 1,2,4,5,6**

Sofosbuvir 400mg /velpatasvir 100mg (Epclusa)

12 weeks

**Genotype 3 patients require NS5A resistance associated substitution (RAS) testing to look for Y93H substitution*

AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.

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Monitoring on Treatment

- Most common side effects: headache, fatigue, nausea, insomnia
- On treatment HCV RNA and routine labs not needed for most
  - Periodic liver enzyme testing for patients with cirrhosis
  - Periodic liver enzyme and HBV testing for those with HBV coinfection
- Baseline HCV RNA and 12 weeks after completing therapy

Sustained virologic response (SVR) 12: negative viral load 12 weeks after completion of therapy

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Hepatitis C Treatment: Special Populations

Population	Considerations
Decompensated cirrhosis	Avoid regimens with protease inhibitors Consider referral to liver transplant center
DAA Treatment Failure	Sofosbuvir/velpatasvir/voxilaprevir x 12 weeks
Renal insufficiency	No DAA dose adjustments required when using recommended regimens Dose adjustment of Ribavirin
HCV-HBV Coinfection	Risk of HBV reactivation during HCV treatment → monitor HBV DNA in patients with +HBsAg vs. prophylactic treatment during therapy
HCV-HIV Coinfection	Many drug-drug interactions HIV therapy should *not* be paused to allow for HCV treatment
Pregnancy	HCV treatment *not* currently recommended during pregnancy

Wang C et al. Clin Gastroenterol Hepatol. 2017;15:132-136.
AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care.

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Follow-Up After Cure

Follow-up For Patients Who Achieve SVR	
Recommendation	**Rating**
For patients without advanced fibrosis (F0-F2), routine follow-up as if they were never infected with HCV	I, B
Assess for HCV recurrence only if patient has risk factors for reinfection or new unexplained hepatic dysfunction. Use HCV RNA.	I, A
Surveillance for hepatocellular carcinoma for patients with advanced fibrosis (F3-F4).	I, B

Patients should be counseled they remain susceptible to re-infection.

AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. HCV testing and linkage to care. Heimbach JK et al. Hepatology 2018;67:358-80.

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HCV Treatment: Evolving Provider Roles

HCV eradication will require engagement of multiple healthcare provider groups

Shifting role of hepatology providers in HCV treatment:

- Advanced liver disease / decompensated cirrhosis
- DAA treatment failures
- Hepatocellular carcinoma
- HBV-HCV coinfection
- Liver transplantation

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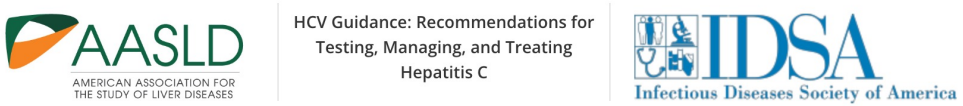
Helpful Resources

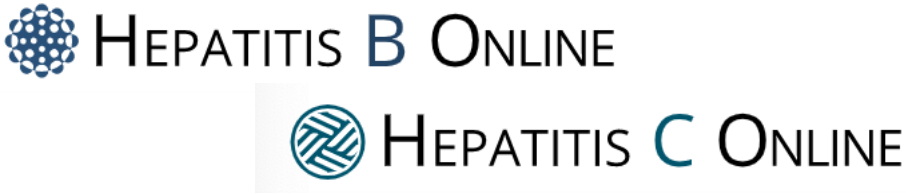
AASLD/IDSA Guidelines

hcvguidelines.org



Hepatitis B & C Online

hepatitisb.uw.edu
hepatitisc.uw.edu



Project ECHO

Tuesdays 12:00-1:15

Contact Pam Landinez
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Questions?

Acknowledgement

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,098,654 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program Mountain West