Viral Hepatitis B and C

April 25th, 2025

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Disclosures/Conflict of Interest

- I have no financial relationships or conflict of interest to disclose regarding materials discussed in the presentation
- Slides courtesy Dr. Joseph Ahn and Dr. Dekey Lhewa

Viral Hepatitides

Session Objectives

1. Understand the epidemiology and natural history of hepatitis B and C
2. Identify chronic infection with hepatitis B and C
3. Identify the main routes of transmission/risk factors of viral hepatitis B and C
4. Interpret the various laboratory tests used to diagnose viral hepatitis B and C

Viral Hepatitides

Overview

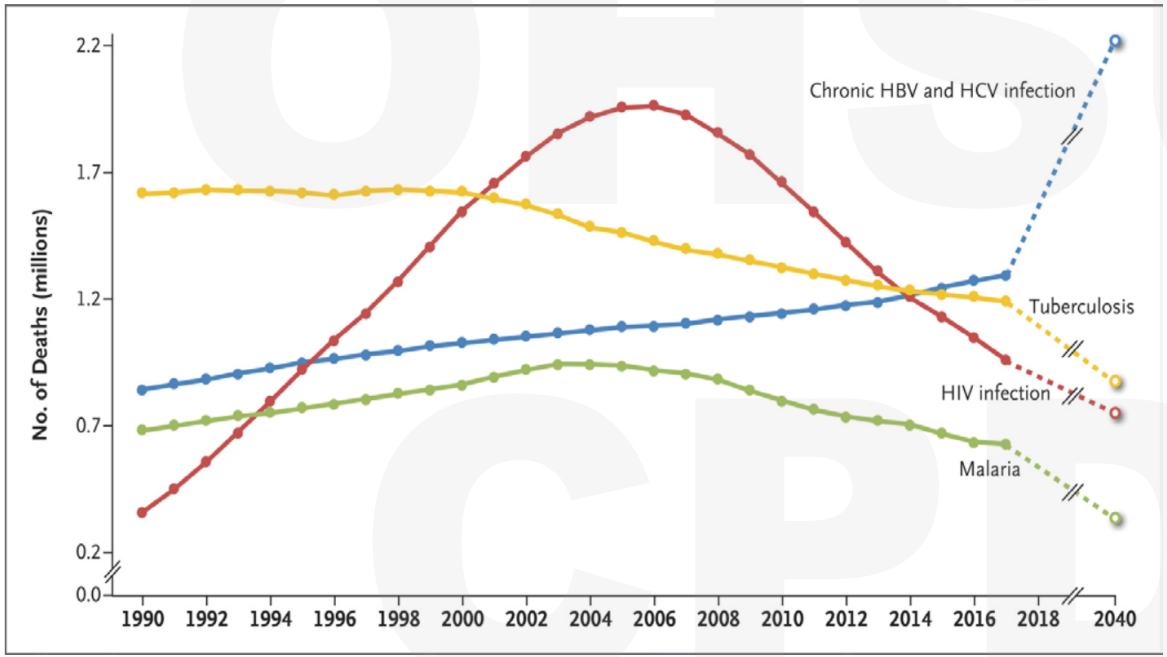
1. General features

2. HCV

3. HBV

Viral Hepatitides

Relevance



In the US from 2003-2013: The number of HCV-associated deaths exceeded that of the top 60 other notifiable infectious conditions **combined**

www.cdc.gov
CDC HCV Elimination-strategic plan 2016-2020

Ly KN, et al. *Clin Infect Dis*, 2016.
Thomas, DL NEJM 2019

Viral Hepatitides

General Overview

	Type of Hepatitis				
	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces *(blood)*
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	(yes)
Prevention	pre/post-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

Viral Hepatitides

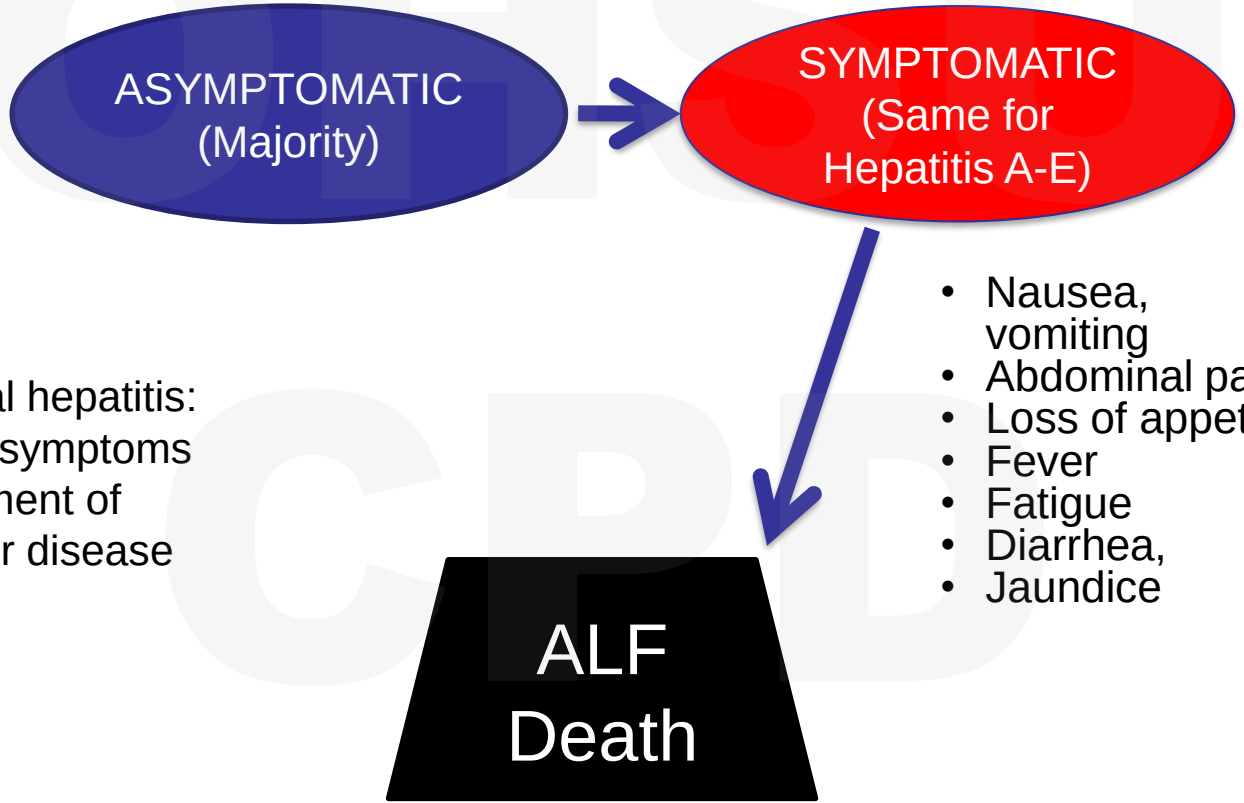
HBV, HCV, HDV Transmission- Think BLOOD

- **Percutaneous** (passage through the skin) exposures to infected blood
  - Injection drug use
  - Blood products (rare in US after 1992)
  - Therapeutic (contaminated equipment e.g., endoscopy, hemodialysis; unsafe injection practices e.g., multiple dose medication vials, therapeutic injections) usually recognized in context of outbreaks
  - Occupational (needlestick injury)
  - Sharing personal items contaminated with infected blood, e.g., razors or toothbrushes (inefficient vectors of transmission)
- Permucosal
  - Perinatal
  - Sexual

MMWR

Viral Hepatitides

Acute Hepatitis- Signs & Symptoms

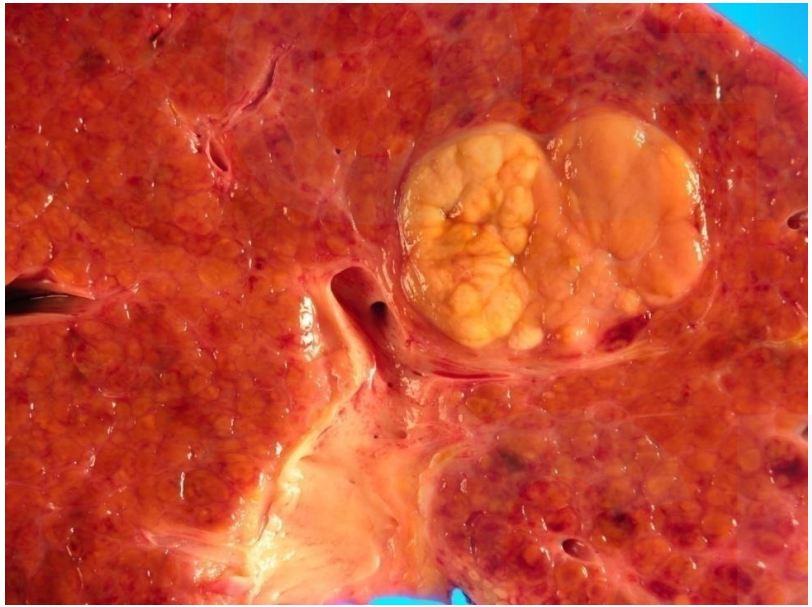


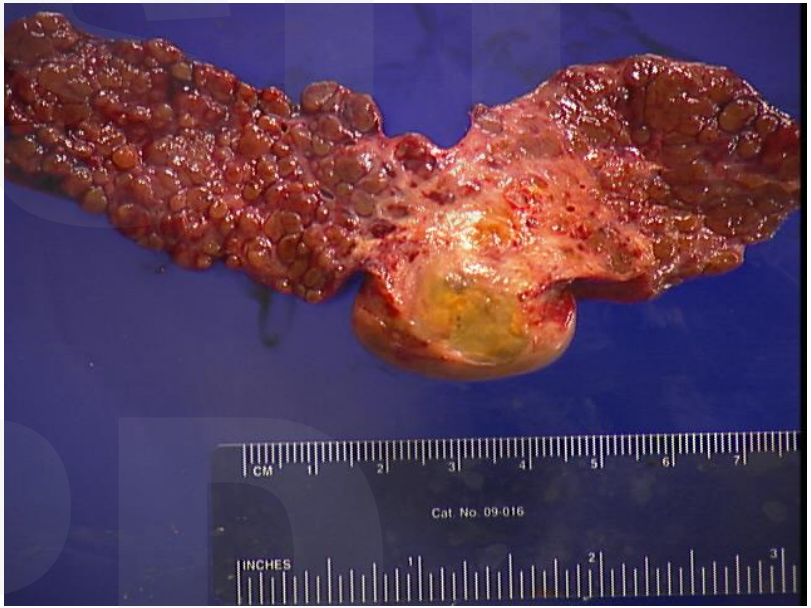
- Nausea, vomiting
- Abdominal pain
- Loss of appetite
- Fever
- Fatigue
- Diarrhea,
- Jaundice

In chronic viral hepatitis: frequently no symptoms until development of advanced liver disease

Viral Hepatitides

Hepatitis B, C, D= Carcinogens





= Cirrhosis + Liver Cancer

Viral Hepatitides

Extrahepatic Manifestations of Acute Viral Hepatitis

Vasculitis- PAN, Cryoglobulinemia

Arthritis

HEME- thrombocytopenia, Red Cell Aplasia, HA

CNS- Transverse myelitis, neuropathy

Renal- CKD, MGN

DERM

Viral Hepatitides

Overview

1. General features
2. **HCV**
3. HBV

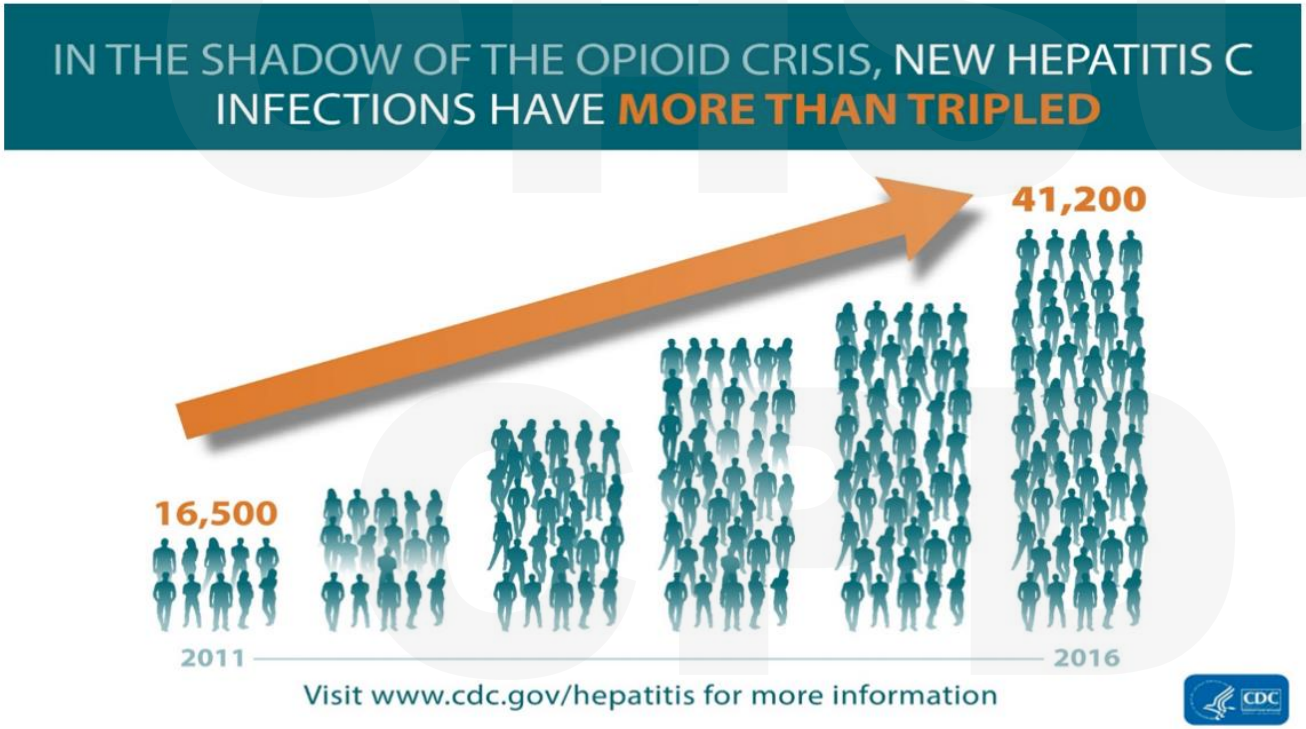
Viral Hepatitides

Why is HCV still important in 2022?

- An estimated 2.4 million people in the US were living with Hepatitis C during 2013-2016
- Health care disparity
  - Disproportionately impacts marginalized populations
  - Underinsured, people who inject drugs (PWID), HIV+, minorities
- Revolution in HCV eradication has occurred
- No vaccine
- Treatment leads to “Cure”
- Resurgent incidence due to opioid epidemic

MMWR. CDC 2020

Changing Epidemiology of HCV



Impact of Covid?

Viral Hepatitides

Hepatitis C: Clinical Features

- **Incubation period**
  - Average 6-8 wks, Range 2-26 wks
- **Acute illness**
  - Subclinical, anicteric, symptoms If occur, often non-specific
- **Chronic infection**
  - 75-85% (ineffective immune response)
  - Most asymptomatic until late disease

Viral Hepatitides

HCV Tests

- Screening tests with antibody to HCV (anti-HCV) = HCV Ab
  - Positive result means exposure
- Nucleic Acid tests for the virus and amount of virus = HCV RNA
  - Detectable virus means
    - chronic infection if documented over time, else
    - acute infection with resolution/clearance if viremia resolves over first few months of infection

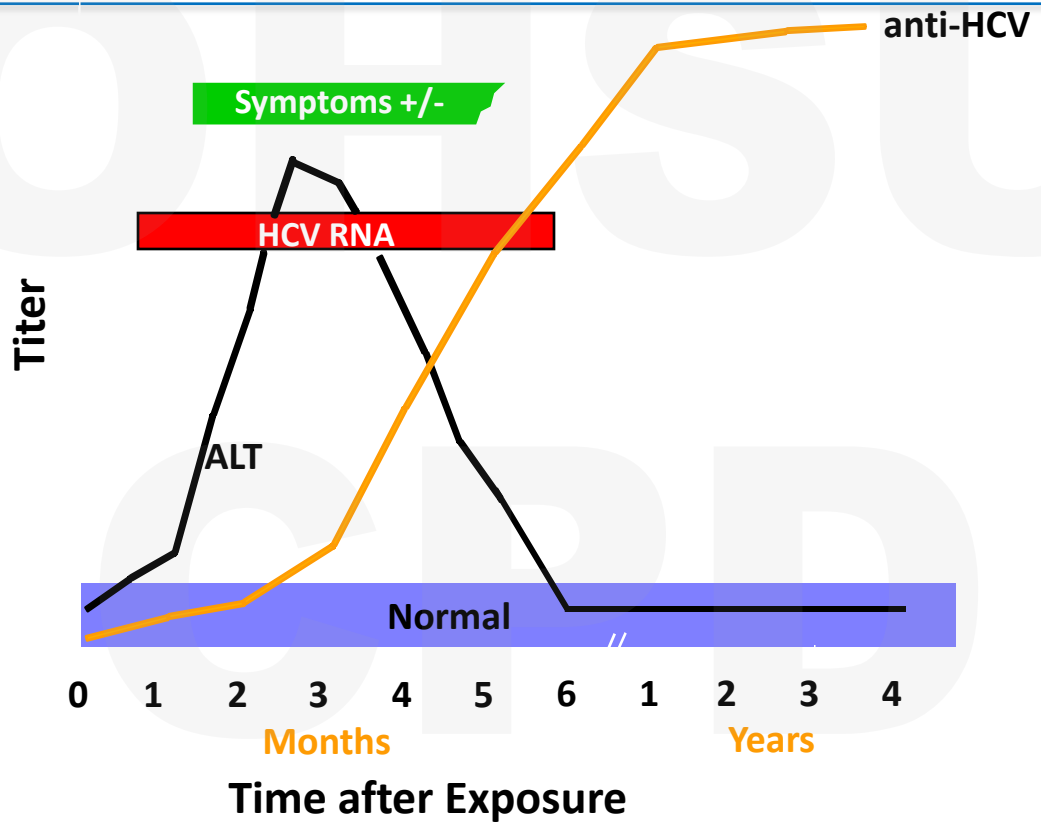
Viral Hepatitides

HCV Test Interpretation

Anti-HCV	HCV RNA	Interpretation
+	+	**Acute or chronic HCV depending on the clinical context**
+	–	**Resolved infection** False positive HCV antibody Low-level intermittent viremia
–	+	**Early acute HCV infection** Chronic HCV in setting of immunosuppressed state
–	–	**Absence of HCV infection**

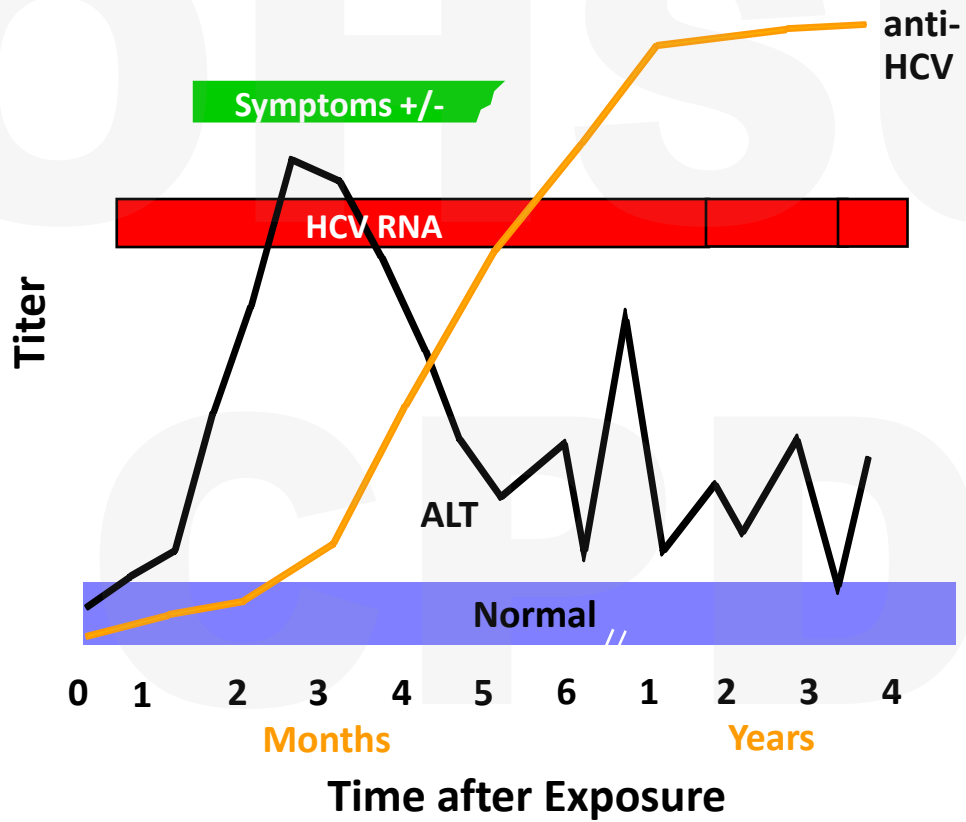
Viral Hepatitides

Acute HCV with Recovery



Viral Hepatitides

Chronic HCV



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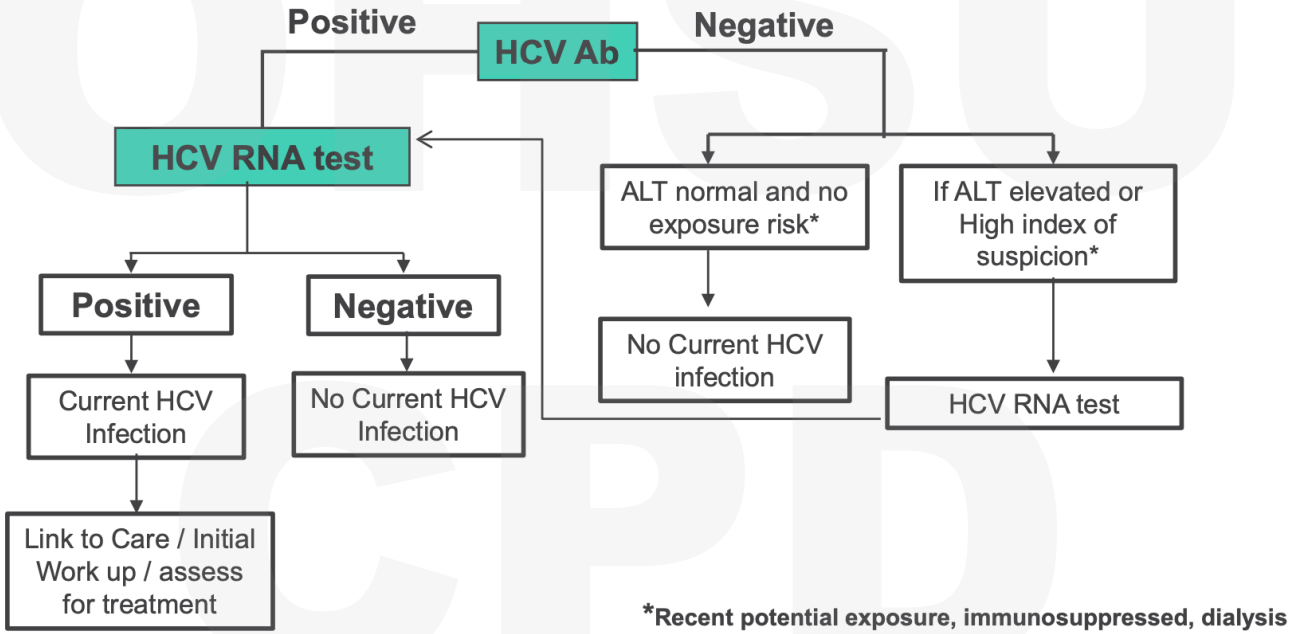
Diagnostic Testing



Source: CDC. Testing for HCV Infection: An update of guidance for clinicians and laboratories. MMWR 2013;62(18).

Viral Hepatitides

Natural History

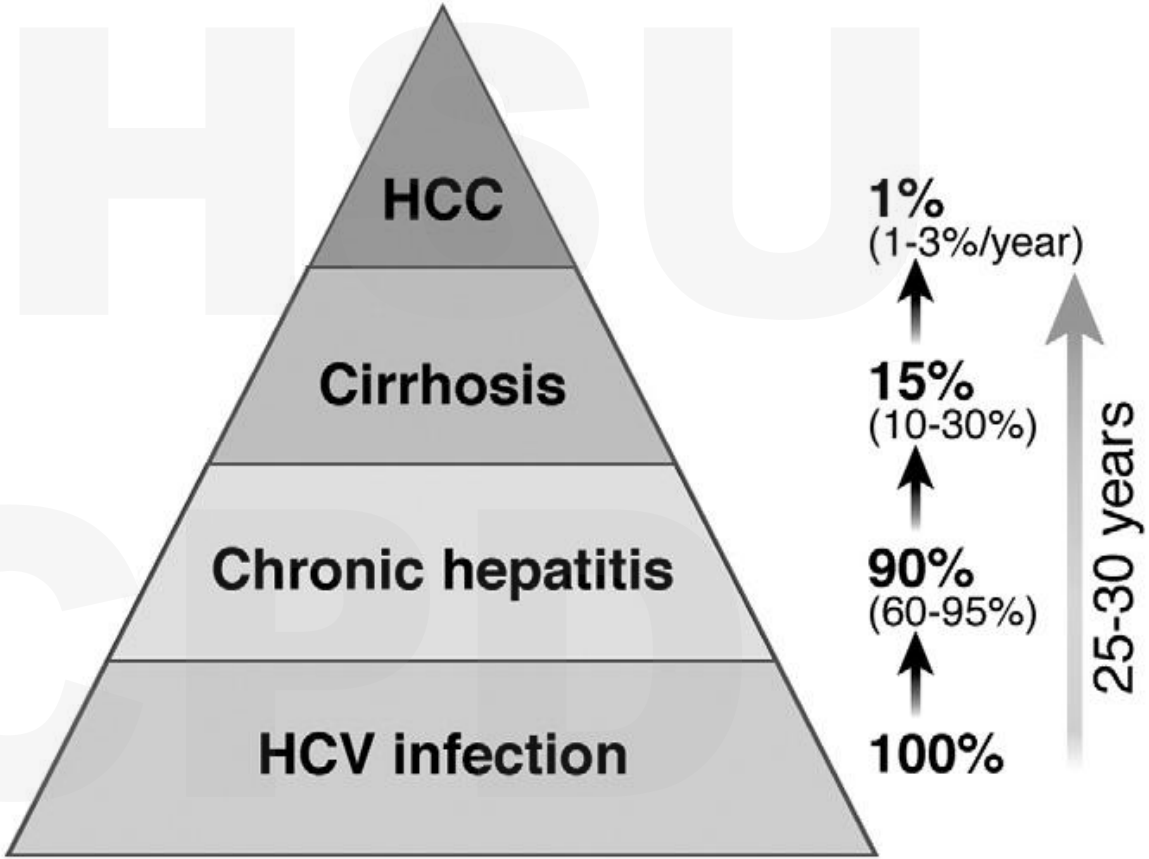
Factors Associated with Fibrosis Progression

Increased alcohol intake

Age > 40 years at time of infection

Immune suppression: HIV co-infection, post-liver transplant

Chronic HBV co-infection



El Serag, Gastro 2007

Viral Hepatitides

HCV Screening Recommendations (AASLD/CDC/USPSTF)

- **One-time test for HCV (regardless of risk factors) with HCV antibody**
  - **All adults ≥ 18 yo**

- All pregnant women during each pregnancy except if prevalence of HCV infection is <0.1%

- At risk persons to be tested for HCV infection
  - Injected illegal drugs (past and current)
  - Selected medical conditions: ESRD, HIV, STDs
  - Prior recipients of transfusions or organ transplants
  - Children born to HCV-infected mothers
  - Health care, emergency medical and public safety workers after needle sticks, sharps, or mucosal exposure to HCV-positive blood

Ghany MG, et al. *Hepatology*. 2009;49:1335-1374
CDC. *MMWR.* 2020; 69:1-17
JAMA 2020

Therapy- HCV Can Be Cured in Most Patients

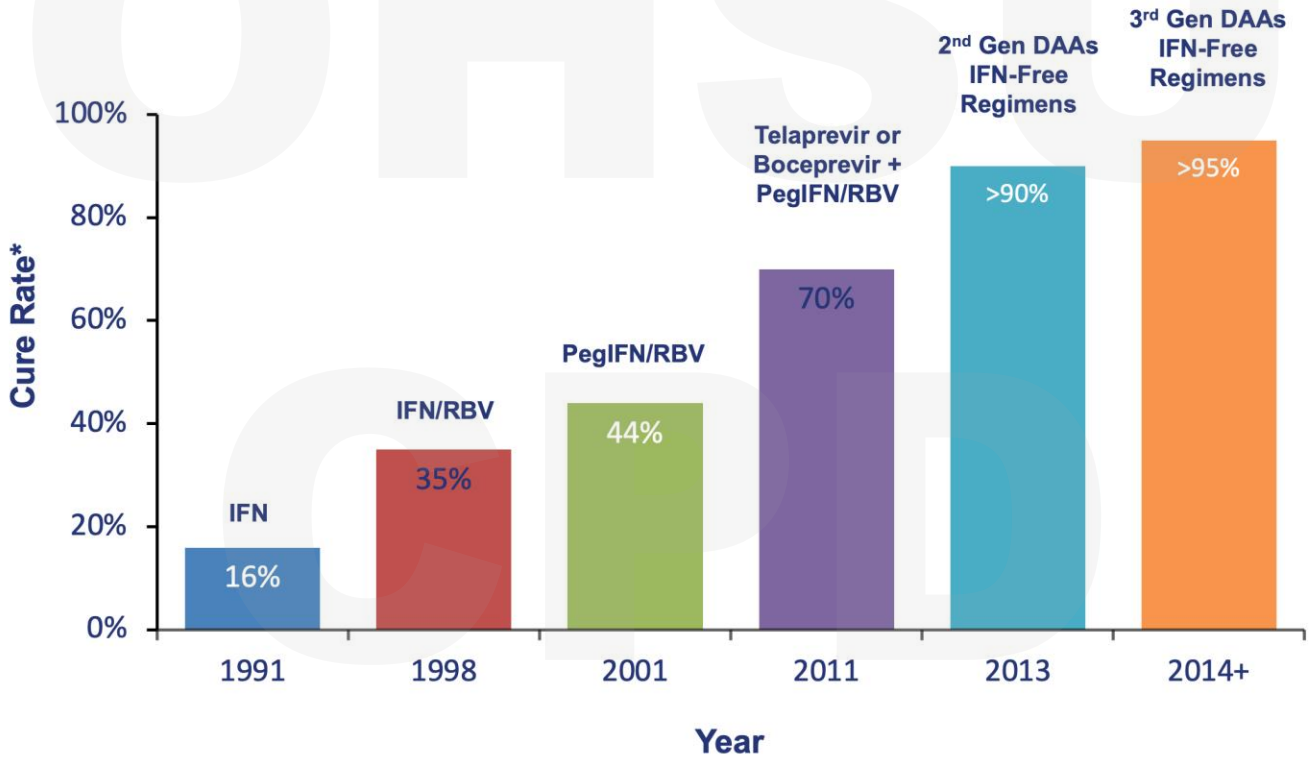
- Unlike HBV and HIV, HCV is a **curable** disease
  - 90-100% cure rates, even in difficult to treat patients: cirrhotic, ESLD, dialysis
- Cure→ durable; leads to lower liver cancer, cirrhosis, mortality risk
- How do we define “cure”?

  = Undetectable HCV RNA 12 weeks after Rx completion

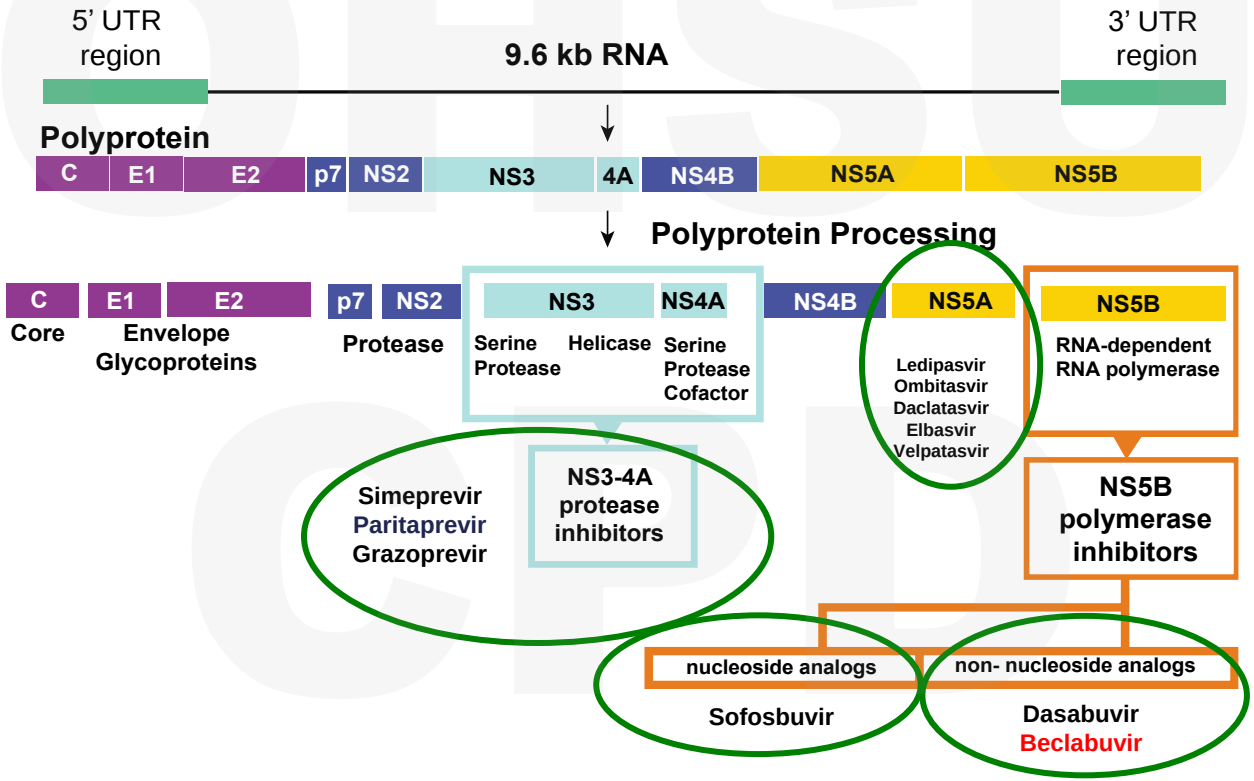
  = Sustained virological response (SVR)

Viral Hepatitides

Rising Cure Rates for HCV



Multi-targeted Approach for Treatment: Approved Protease, Polymerase and NS5A Inhibitors



Adapted from McGovern B, Abu Dayyeh B, and Chung RT. *Hepatology*. 2008; 48:1700-12

Viral Hepatitides

Management

Product	Brand Name	HCV Genotype	Dosing (weeks)
Glecprevir/pibrentasvir	Mavyret	1-6	QD x 8-16
Sofosbuvir/velpatasvir/ voxilaprevir	Vosevi	1-6	QD x 12
Sofosbuvir/velpatasvir	Epclusa	1-6	QD x 12
Elbasvir/grazoprevir	Zepatier	1,4	QD x 12-16
Ledispasvir/sofosbuvir	Harvoni	1, 4-6	QD x 8-24

HBV Reactivation risk assessment in All

Decompensated

No Protease Inhibitors

HBV Reactivation

- FDA report: 29 cases HBV reactivation with DAA therapy
- Management
  - Check HBV serologies
  - HBsAg +, +HBV DNA meets criteria for tx
  - HBsAg -, HBcAb+, HBsAb+/-: Consider monitoring

Post-Treatment Management

- HCV antibody will remain positive
- Can be infected again- annual testing for at risk individuals
- Substance abuse treatment referral
- Co-existing disease or advanced fibrosis (F3-4)
  - Disease specific therapy
  - Surveillance for liver cancer

Viral Hepatitides

Overview

1. General features
2. HCV
3. **HBV**

Viral Hepatitides

HBV Epidemiology Summary

~ 257-295 million worldwide, > 67% from Africa, Western Pacific

2.4 M in US

- Acute HBV rising in US since 2014

Majority of persons with HBV are unaware

< 2% of candidates are on Rx

Only about 1 in 4 adults are fully immunized

> 25% die prematurely of HCC, cirrhosis, ESLD

Wong et al., Hepatology 2021

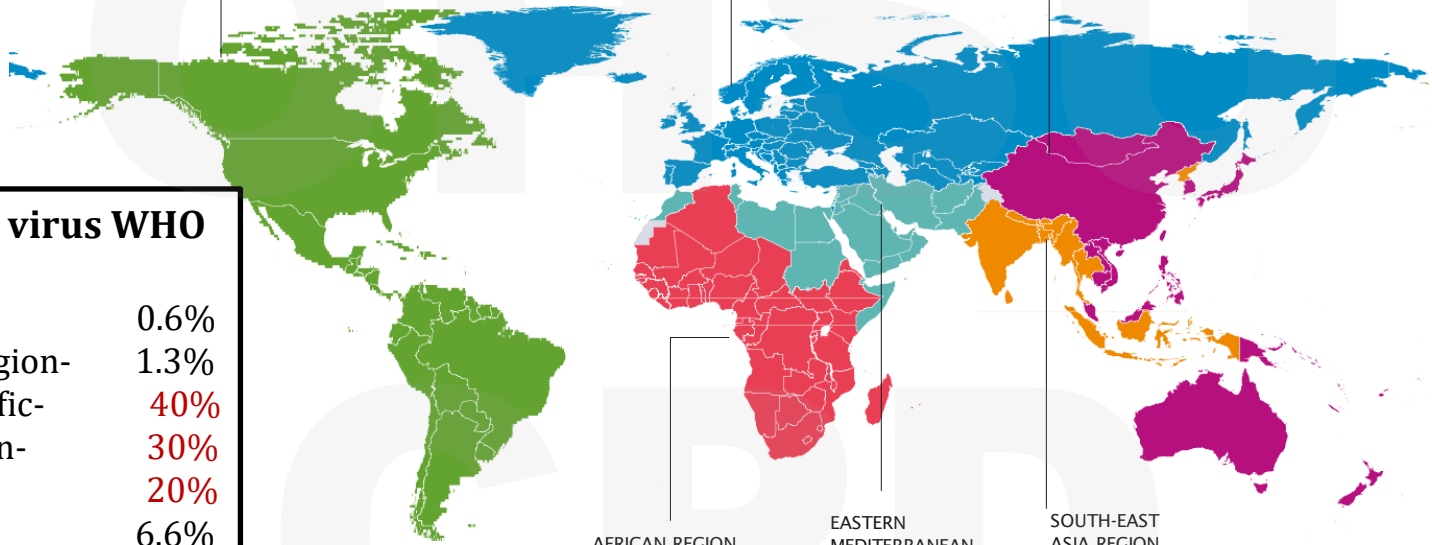
Burden of Hepatitis B virus infection by WHO Region, 2019

2021 Global progress report for viral hepatitis and implications for Africa

REGION OF THE AMERICAS
5,358,907
(3,062,233 - 12,248,931)

EUROPEAN REGION
13,604,235
(10,203,176 - 22,106,882)

WESTERN PACIFIC REGION
115,749,203
(95,213,054 - 141,886,119)



AFRICAN REGION
82,302,593
(62,064,250- 114,683,941)

EASTERN MEDITERRANEAN REGION
18,243,217
(14,373,443 - 23,771,464)

SOUTH-EAST ASIA REGION
60,458,777
(45,344,083 -120,917,554)

Hepatitis B virus WHO regions

Americas-	0.6%
European Region-	1.3%
Western Pacific-	40%
African region-	30%
SEARO-	20%
EMRO-	6.6%

WHO REGIONS
- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region
- Not applicable

Source: WHO, 2021.

GLOBAL
295,852,053
(228,228,727 - 422,645,790)

Progress report on HIV, viral hepatitis and sexually transmitted infections 2021: accountability for the global health sector strategies, 2016–2021: actions for impact. Geneva: World Health Organization; 2021

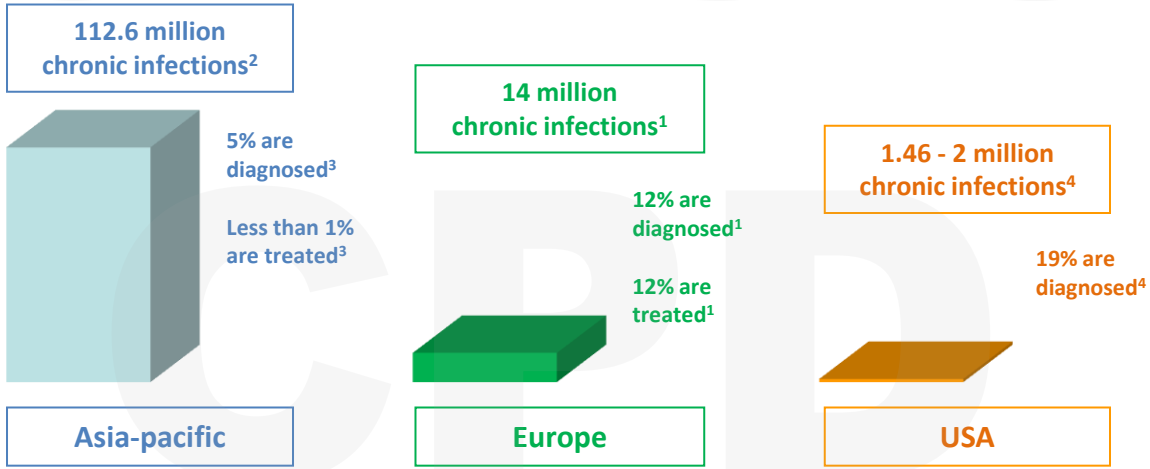
Hepatitis B (HBV)- the Facts

- #1 worldwide liver infection
  - Not curable
  - 100x infectious > HIV
  - 10x infectious > HCV
- Blood and bodily fluid transmission
  - Asymptomatic, slow progression
  - Often undetected for many years

1. Hepatitis Australia. Available at http://www.hepatitisaustralia.com/about_hepatitis/hep_b.html. Accessed April 2009;
2. World Health Organization. Hepatitis B Fact Sheet. Available at http://www.who.int/mediacentre/factsheets/fs204/en/. Accessed April 2009;
3. Ulmer T, et al.(2007) European orientation towards the Better Management of Hepatitis B in Europe .

HBV- an Unmet Medical Need

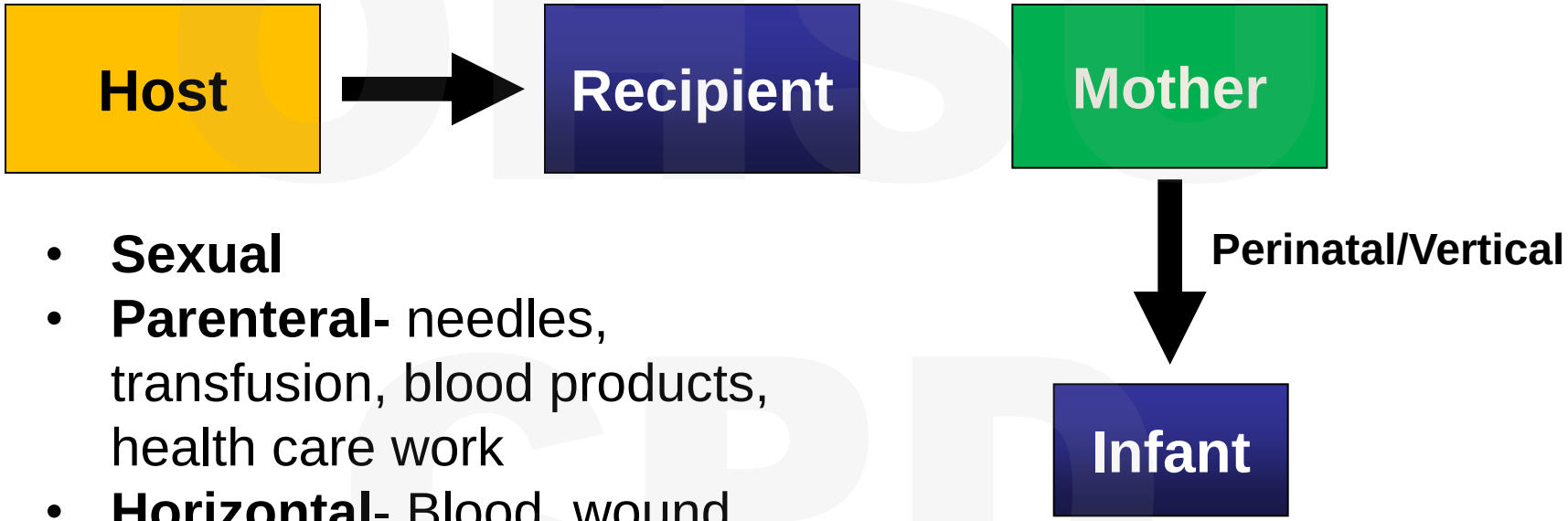
- Under-diagnosed
- Under-treated



1. BMS Market Research. Information available upon request from Bristol-Myers Squibb;
2. Mohamed R, et al. J Gastroenterol Hepatol 2004;19:958-69;
3. Decision Resources. Hepatitis B virus in China – Emerging markets study #5; 4. BMS Market Research.

Viral Hepatitides

HBV Modes of Transmission



- **Sexual**
- **Parenteral-** needles, transfusion, blood products, health care work
- **Horizontal**- Blood, wound, household contact

•No clear risk factors in ~ 20% of patients

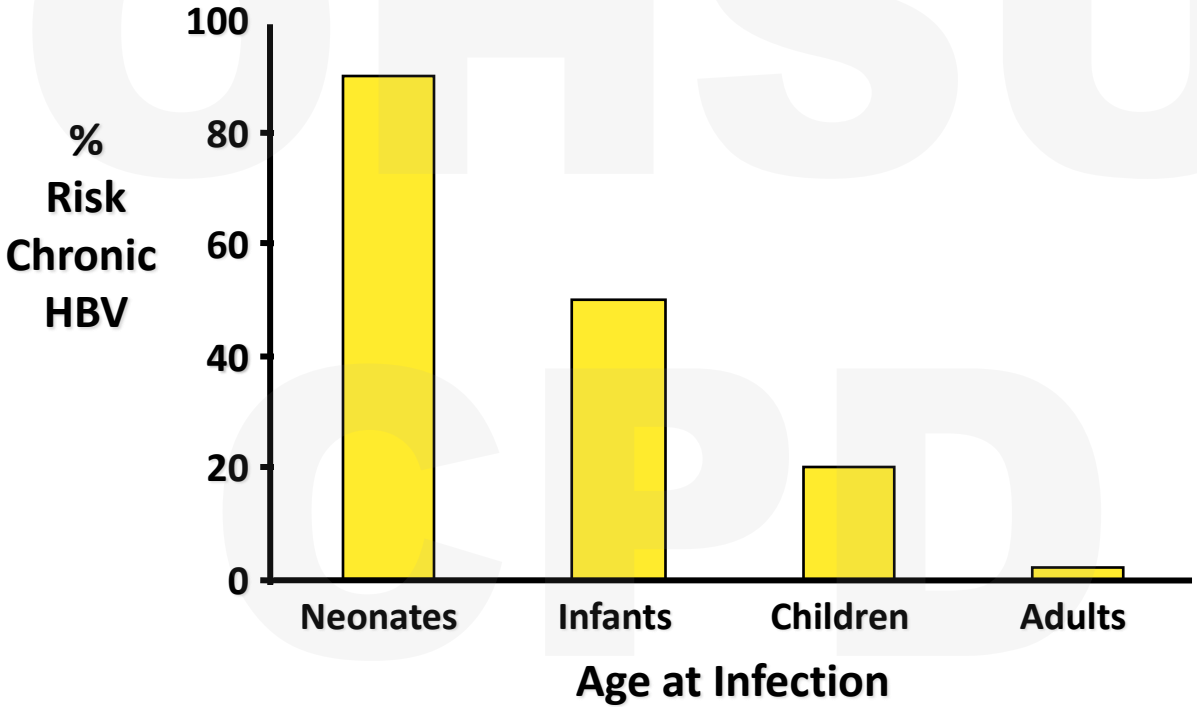
Viral Hepatitides

CDC Screening Recommendations for HBV by Risk Factors

Vertical transmission	Blood transmission
Persons born in countries with 2% or higher HBV prevalence	**Persons who inject drugs**
Pregnant women	**Incarcerated persons**
Infants born to HBV-infected mothers	**Household contacts of HBV-infected persons**
	Persons with end-stage renal disease (including hemodialysis patients)
	Blood and tissue donors
Sexual transmission	**HBV reactivation/liver complication**
Men who have sex with men	Persons requiring immunosuppressive therapy
Sexual contacts of HBV-infected persons	Persons infected with hepatitis C virus
	HIV positive persons
	Persons with elevated ALT levels

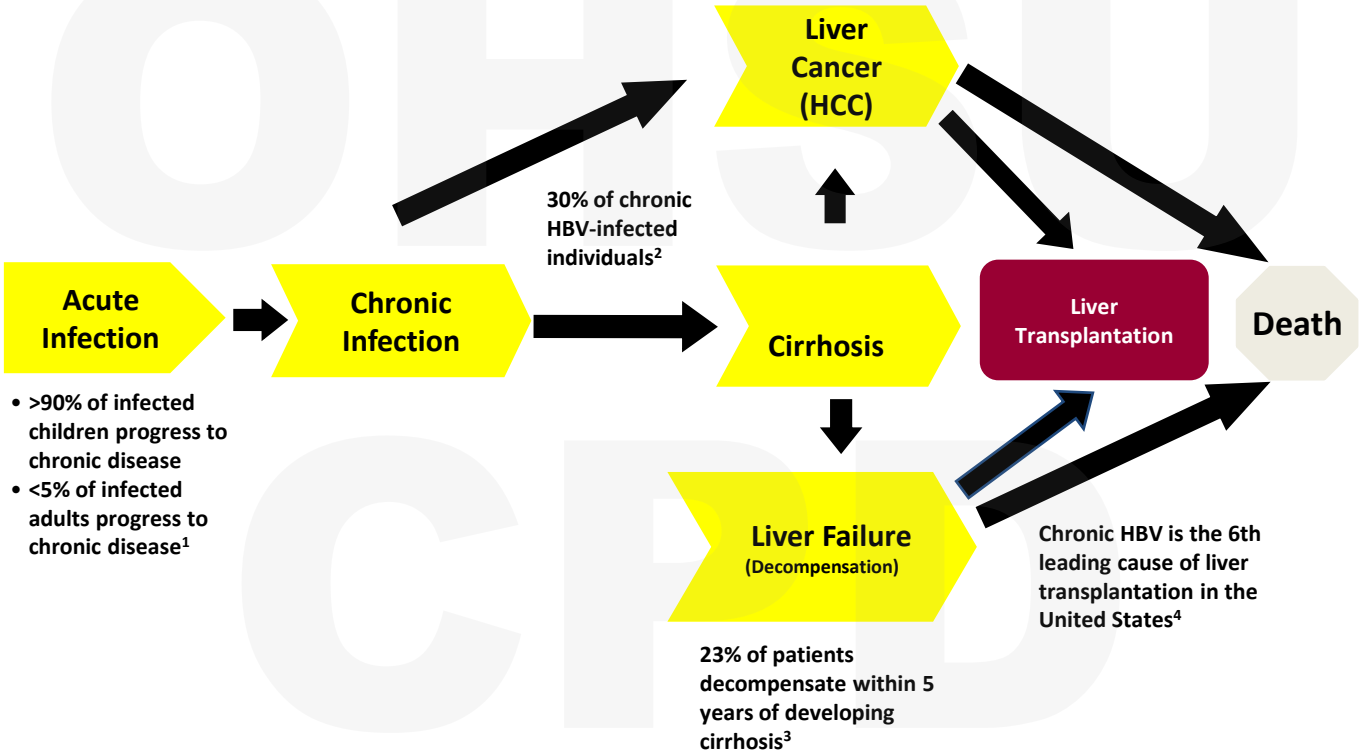
Abara WE, et al. *Ann Intern Med*. 2017;167(11):794-804.

Risk of Chronic HBV Infection is Inversely Related to Age at Infection



J Infect Dis 1985;151:599-603.
Gastroenterology 1987;92:1844-50.
J Gastroenterol Hepatol 2000;15 Suppl:E16-9.

Hepatitis B Disease Progression



Torresi J. *Gastro.* 2000;118:S83-103[1];
Moyer LA *Am J Prev Med.* 1994;10:45-55[2];
Fattovich G. *Hepatology*. 1995;1:77-82[3];
Perrillo RP. *Hepatology*. 2001;33:424-432.[4]

HBV: Phase I Tests

- HBsAg = infection
- Anti-HBs = immunity
  - if anti-HBc is negative
- Anti-HBc = exposure
- Anti-HBcIgM= Acute exposure to HBV

HBV: Phase II Tests

- HBV DNA = risk of progression to HCC / cirrhosis
- Anti-HBe (+) =
  - Inactive disease or
- HBeAg(+) =
- -active disease

Interpretation of HBV Serologies

Serologic Marker Results				Interpretation
HBs Ag	Total Anti-HBc	IgM Anti-HBc	Anti-HBs	
-	-	-	-	Never infected and no evidence of immunization
+	+	+	-	Acute infection
+	+	-	-	Chronic infection
-	+	-	-	Exposure, false positive
-	+	-	+	Exposure and clearance of HBV infection
-	-	-	+	Immune (immunization)

4 Phases of Chronic HBV Infection

1) Immune tolerant/trained phase
   - HBeAg positive
   - High HBV DNA (> 20,000 IU/ml)
   - Normal ALT

N

2) HBeAg-positive chronic hepatitis (immune clearance) – "wild-type"
   - High HBV DNA (> 20,000 IU/ml)
   - High or fluctuating ALT
   - Active inflammation on liver biopsy

Y

Pungpapong S, et al. *Mayo Clin Proc.* 2007;82:967-975.

4 Phases of Chronic HBV Infection (cont.)

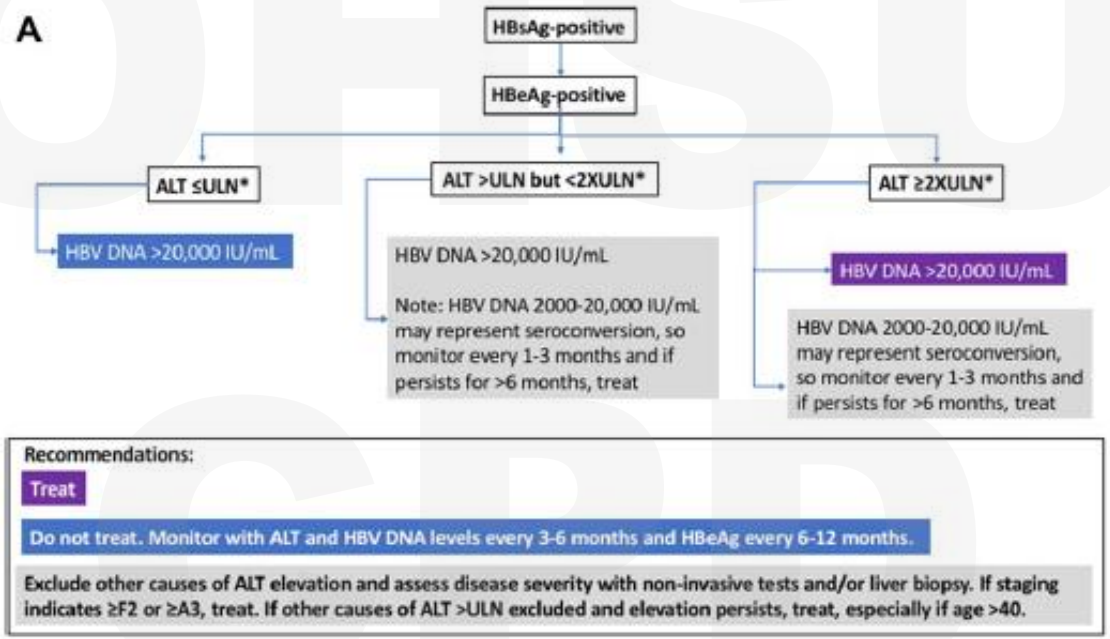
3) Inactive HBsAg carrier (non-replication)
   - HBeAg negative
   - Low HBV DNA (< 2,000 IU/ml)
   - Normal ALT

N

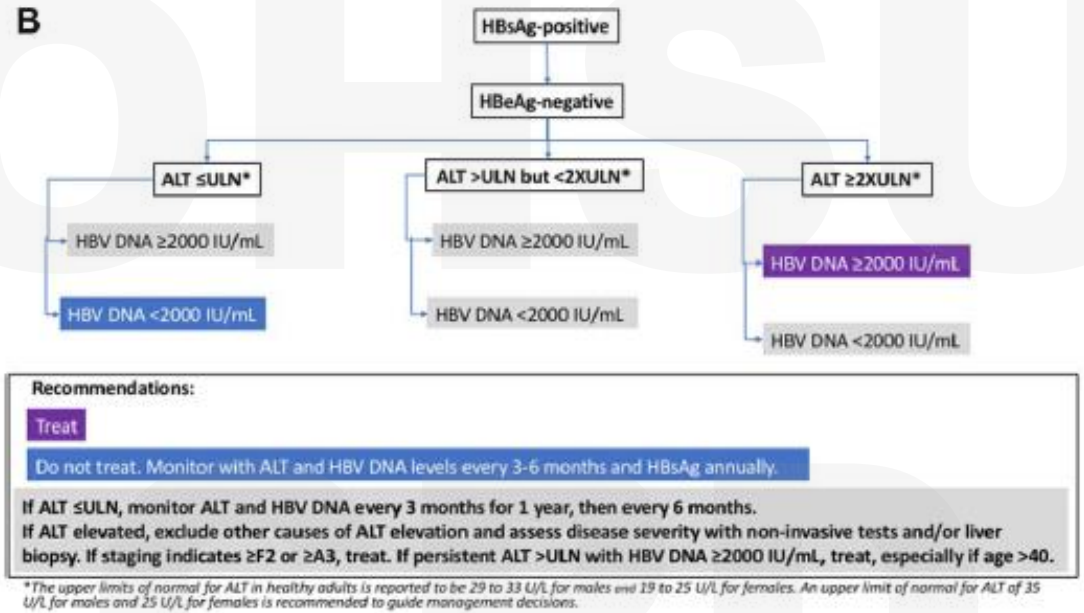
4) HBeAg-negative chronic hepatitis – "pre-core"
   - Intermediate to high HBV DNA (> 2,000 IU/ml)
   - High or fluctuating ALT
   - Active inflammation on liver biopsy

Y

Pungpapong S, et al. *Mayo Clin Proc.* 2007;82:967-975.



AASLD Practice Guidelines TERRAULT ET AL. Hepatology 2018



AASLD Practice Guidelines TERRAULT ET AL. Hepatology 2018

HCC Screening

- 1. All HBsAg-positive patients with cirrhosis should be screened with US examination with or without AFP every 6 months.
- 2. HBsAg-positive adults at high risk for HCC (including Asian or black men over 40 years and Asian women over 50 years of age), persons with a first-degree family member with a history of HCC, or persons with HDV should be screened with US examination with or without AFP every 6 months.

AASLD Practice Guidelines TERRAULT ET AL. Hepatology 2018

HBV Reactivation

Well-Characterized Syndrome

- Abrupt reappearance or rise of HBV DNA in previously inactive or resolved HBV infection
- Often, but not always, accompanied by reappearance of disease activity
- May occur spontaneously or as a result of immunosuppression
- Prevented with HBV treatment, which should continue for at least 1 year after cessation of immunosupression

Potential Consequences

- May lead to clinically apparent acute hepatitis
  - Can be severe
  - Can result in acute liver failure and death
- Many cases are subclinical and resolve spontaneously, or result in persistent infection
- May go undetected until
  - Advanced liver disease is present
  - Disease has been transmitted to sexual or family contacts

Bessone F, et al. *World J Hepatol.* 2016;8:385-394.

Viral Hepatitides

Recommendations for Counseling for Chronic Viral Hepatitis

- NO ETOH
- Hep A vaccine
- Education
  - Household, intimate contacts to be tested & vaccinated
  - Barrier protection until partners can be vaccinated
  - Cover cuts, skin lesions
  - Don’t share toothbrushes, razors, injection equipment
  - Health-care workers- universal precautions

Give thanks. Give life.