

# Viral Hepatitis B and C

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# Viral Hepatitides

## Disclosures/Conflict of Interest

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- 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

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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

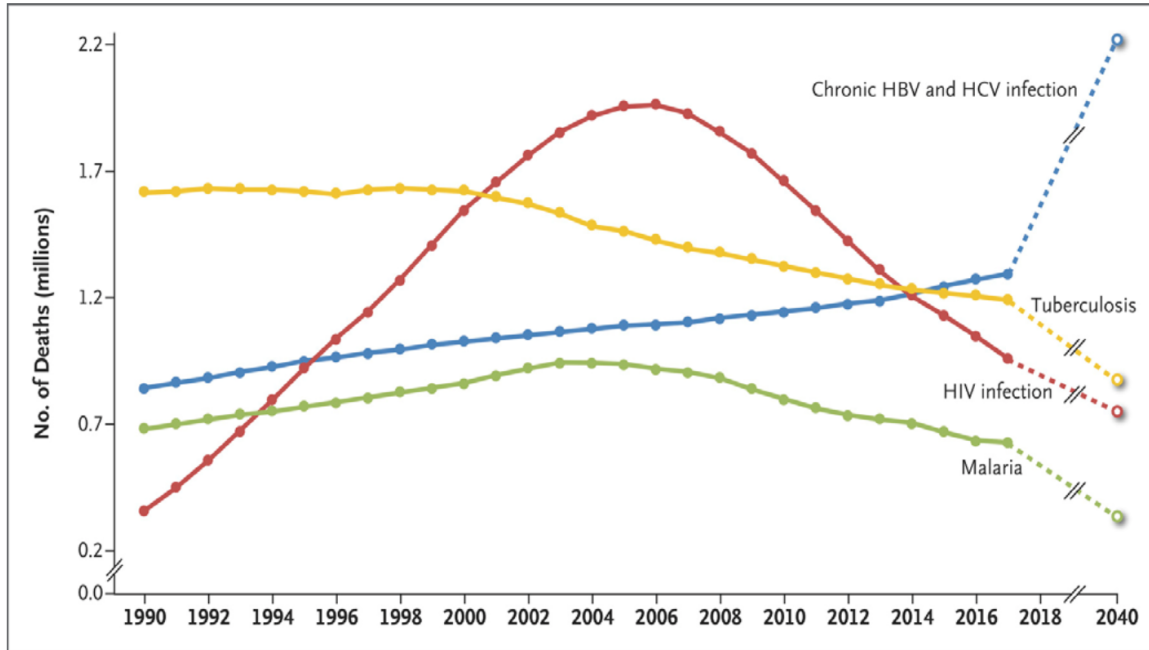
### **1. General features**

2. HCV

3. HBV

# Viral Hepatitis

## 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](http://www.cdc.gov)  
CDC HCV Elimination-strategic plan  
2016-2020

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

# Viral Hepatitis

## 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 ( <i>blood</i> )
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

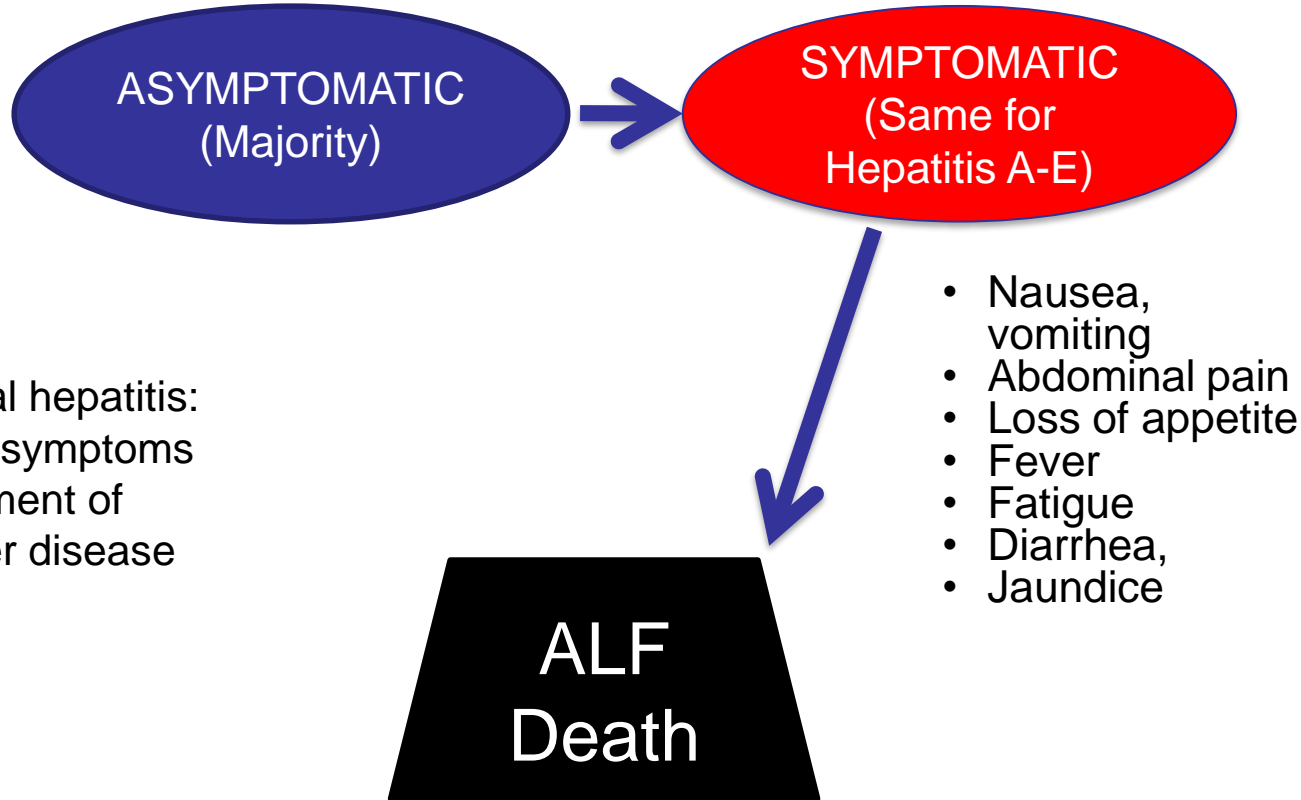
# Viral Hepatitides

## 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)
- **Per mucosal**
  - Perinatal
  - Sexual

# Viral Hepatitides

## Acute Hepatitis- Signs & Symptoms

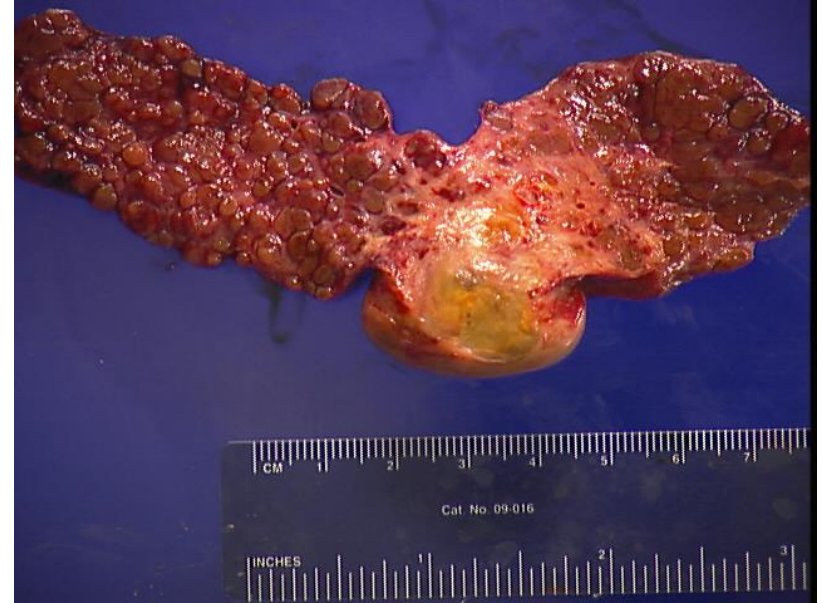
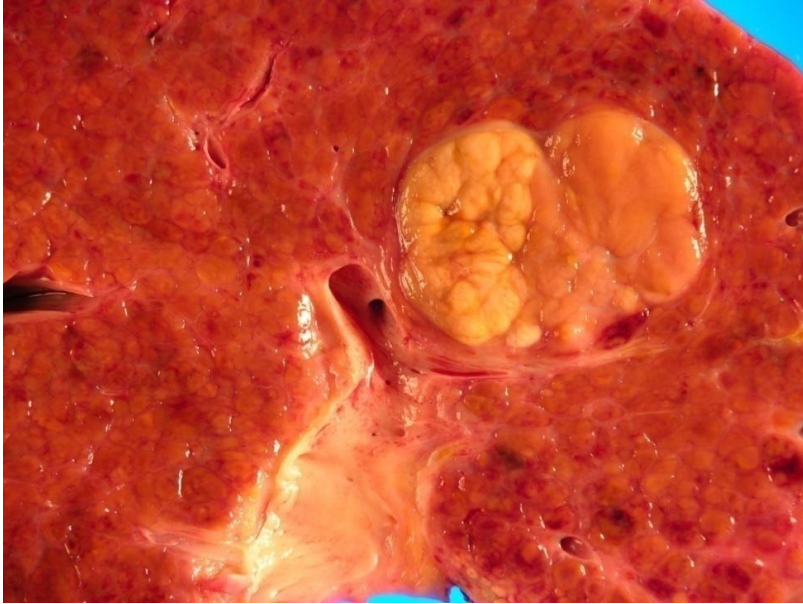


In chronic viral hepatitis:  
frequently no symptoms  
until development of  
advanced liver disease



# 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?

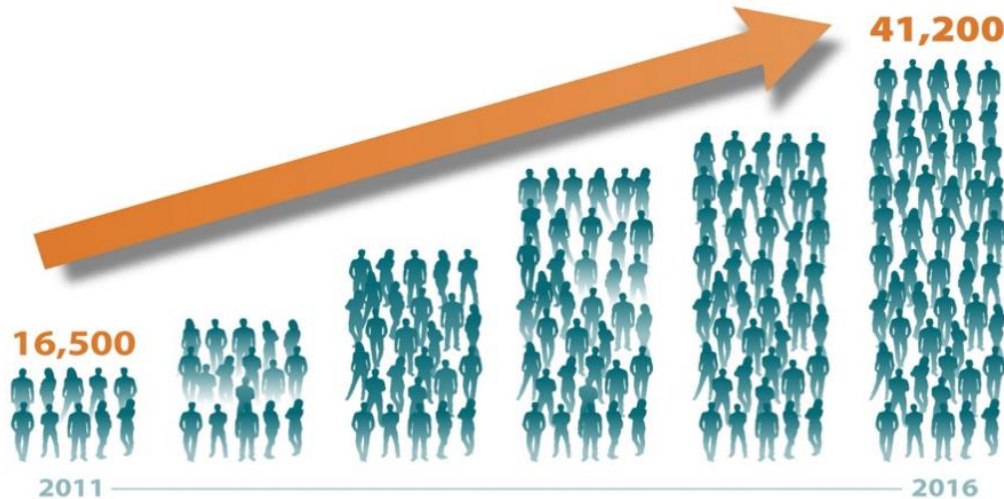
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- An estimated 2.4 million people in the US were living with Hepatitis C during 2013-2016
- Health care disparity
  - Disproportionately impacts marginalized populations
  - Underinsured, people who inject drugs (PWID), HIV+, minorities
- Revolution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

# Viral Hepatitis

## Changing Epidemiology of HCV

IN THE SHADOW OF THE OPIOID CRISIS, NEW HEPATITIS C INFECTIONS HAVE **MORE THAN TRIPLED**



Visit [www.cdc.gov/hepatitis](http://www.cdc.gov/hepatitis) for more information



Impact of  
Covid?

# Viral Hepatitides

## Hepatitis C: Clinical Features

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

# Viral Hepatitides

## HCV Tests

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- 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

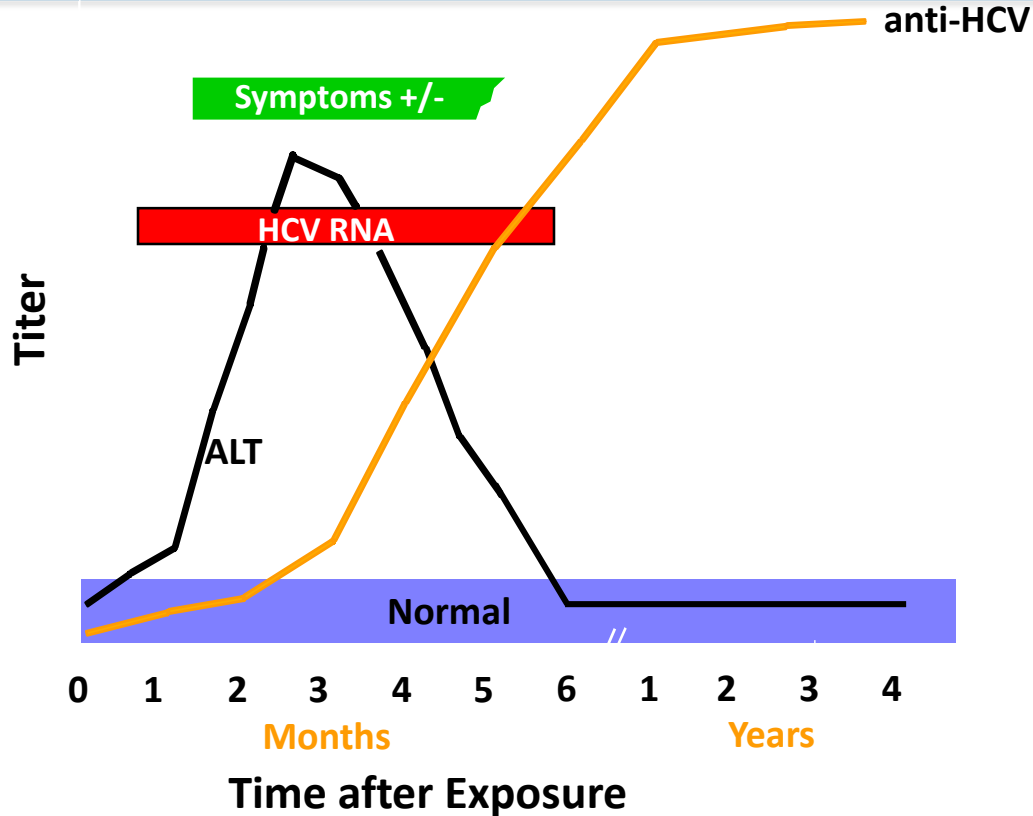
## HCV Test Interpretation

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



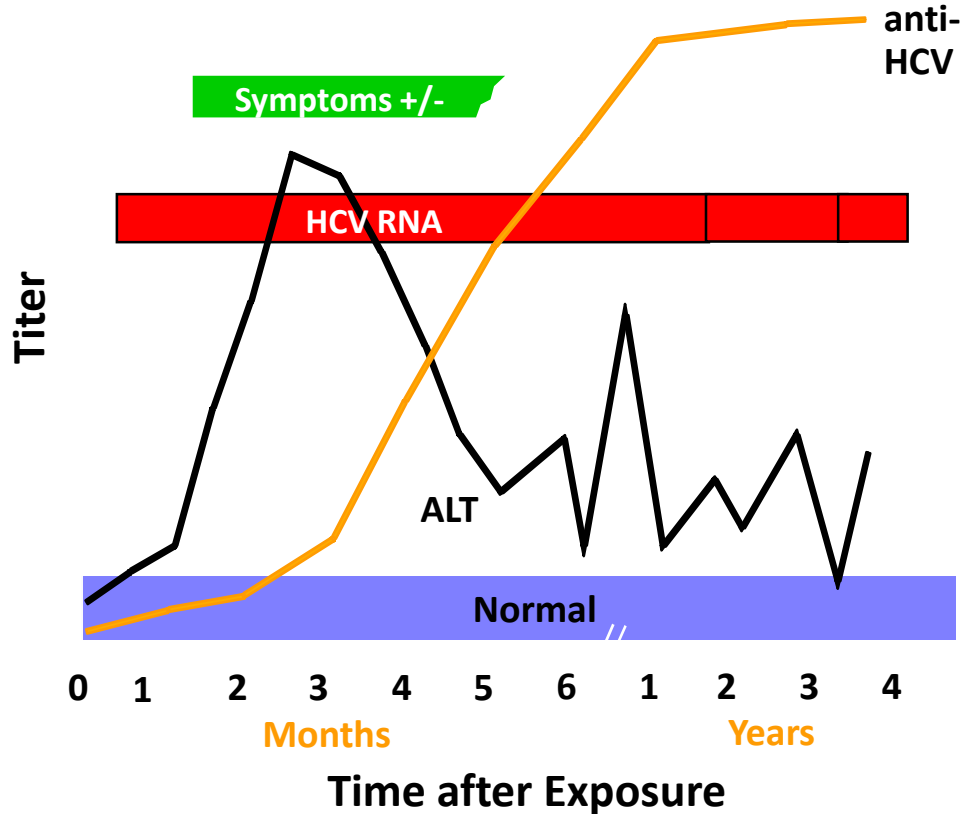
# Viral Hepatitis

## Acute HCV with Recovery



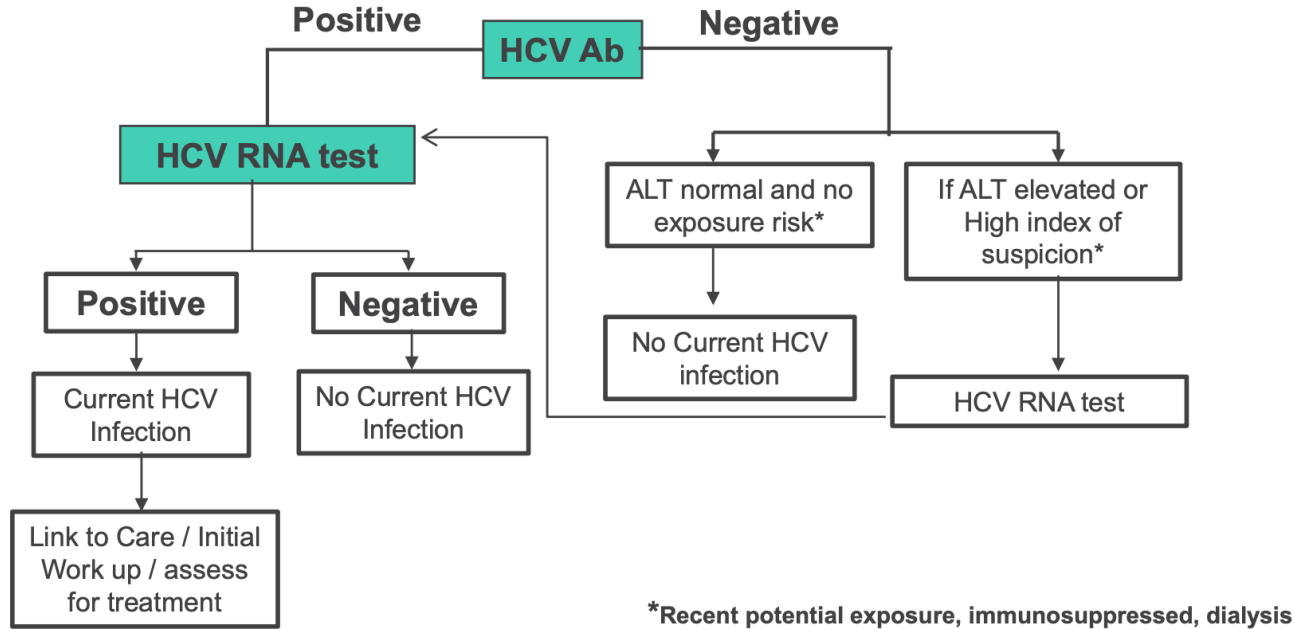
# Viral Hepatitis

## Chronic HCV



# Viral Hepatitis

## Diagnostic Testing



# Viral Hepatitis

## Natural History

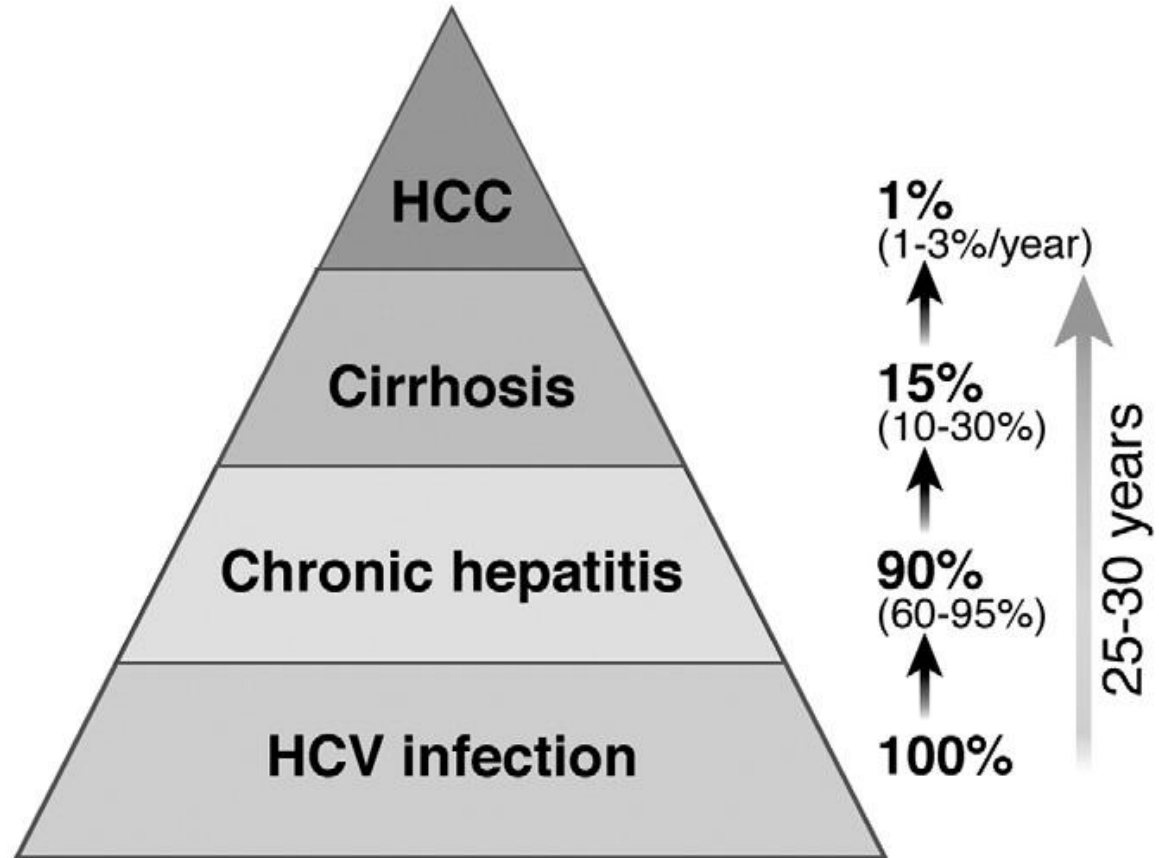
### Factors Associated with Fibrosis Progression

Increased alcohol intake

Age > 40 years at time of infection

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

Chronic HBV co-infection



# Viral Hepatitides

## HCV Screening Recommendations (AASLD/CDC/USPSTF)

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- **One-time test for HCV (regardless of risk factors) with HCV antibody**
  - All adults  $\geq 18$  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

# Viral Hepatitides

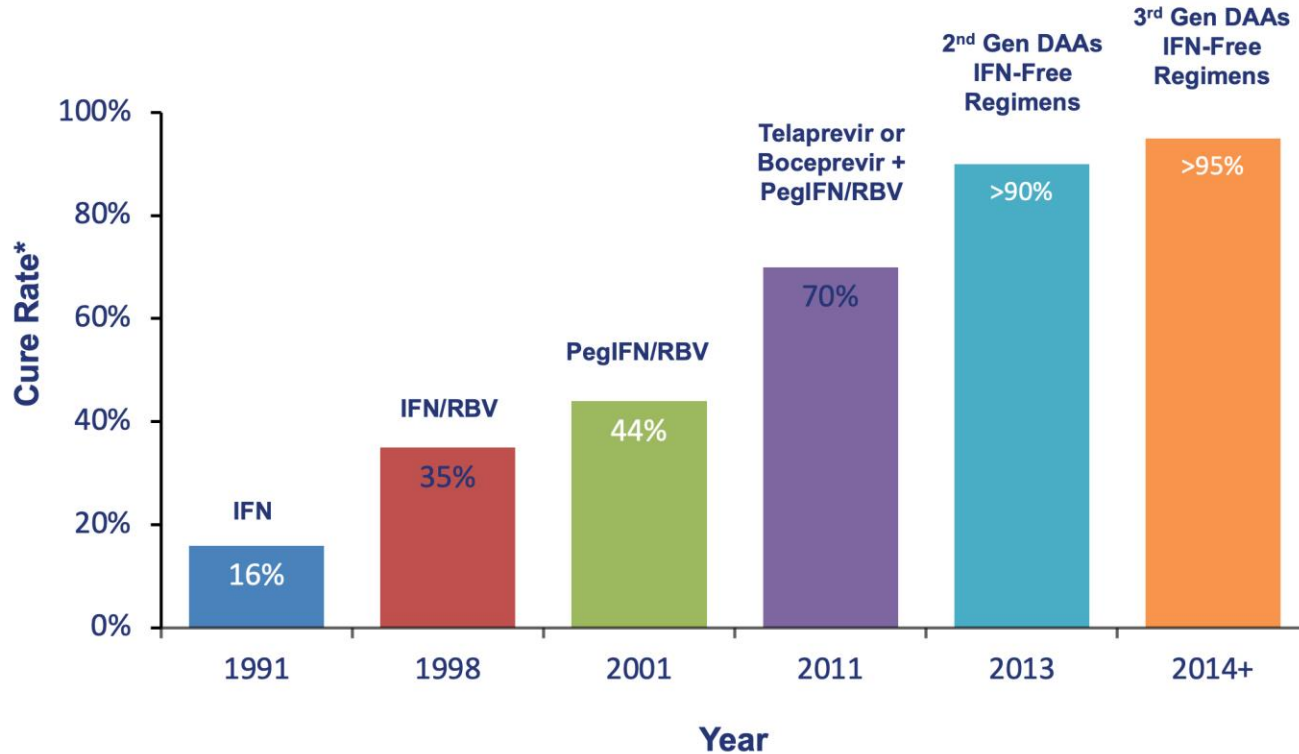
## Therapy- HCV Can Be Cured in Most Patients

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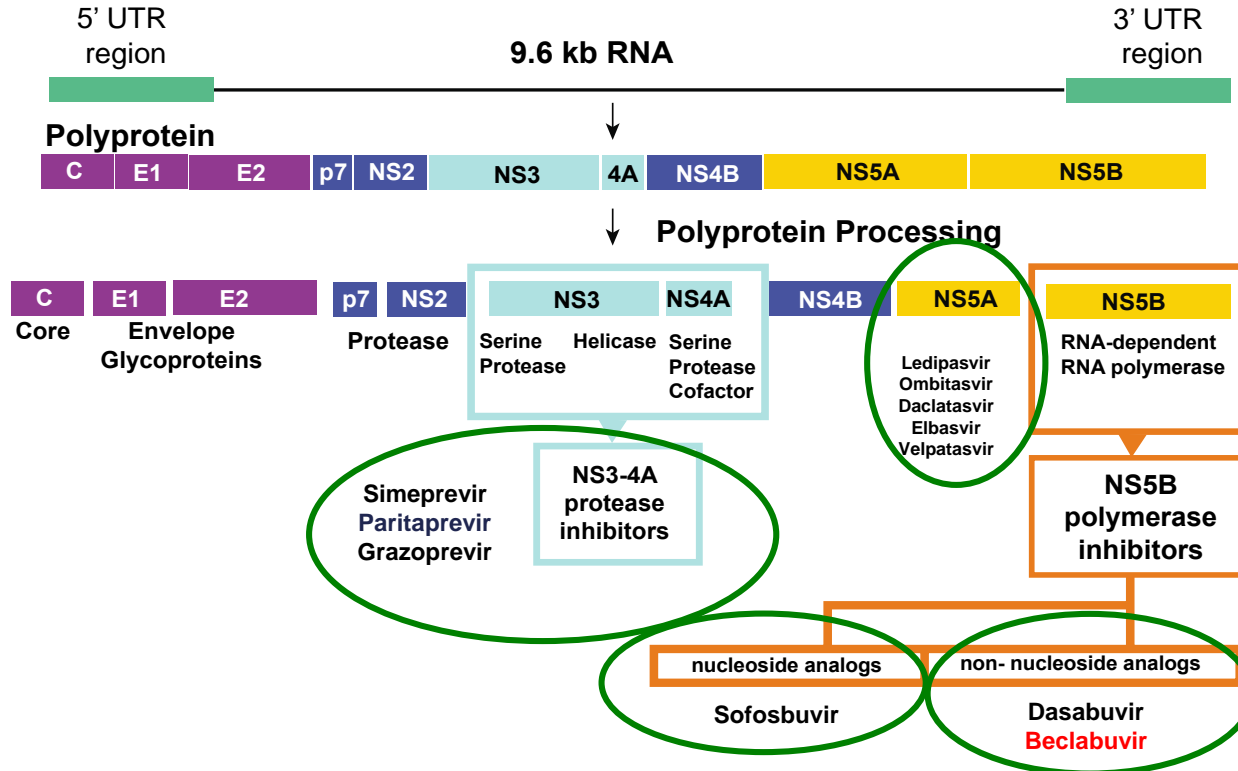
- Unlike HBV and HIV, HCV is a **curable** disease
  - 90-100% cure rates, even in difficult to treat patients: cirrhotic, ESLD, dialysis
- Cure → durable; leads to lower liver cancer, cirrhosis, mortality risk
- How do we define “cure”?
  - = Undetectable HCV RNA 12 weeks after Rx completion
  - = Sustained virological response (SVR)

# Viral Hepatitis

## Rising Cure Rates for HCV



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





# Viral Hepatitides

## Management

Product	Brand Name	HCV Genotype	Dosing (weeks)
Glecaprevir/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
Ledipasvir/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

# Viral Hepatitides

## Post-Treatment Management

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- 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

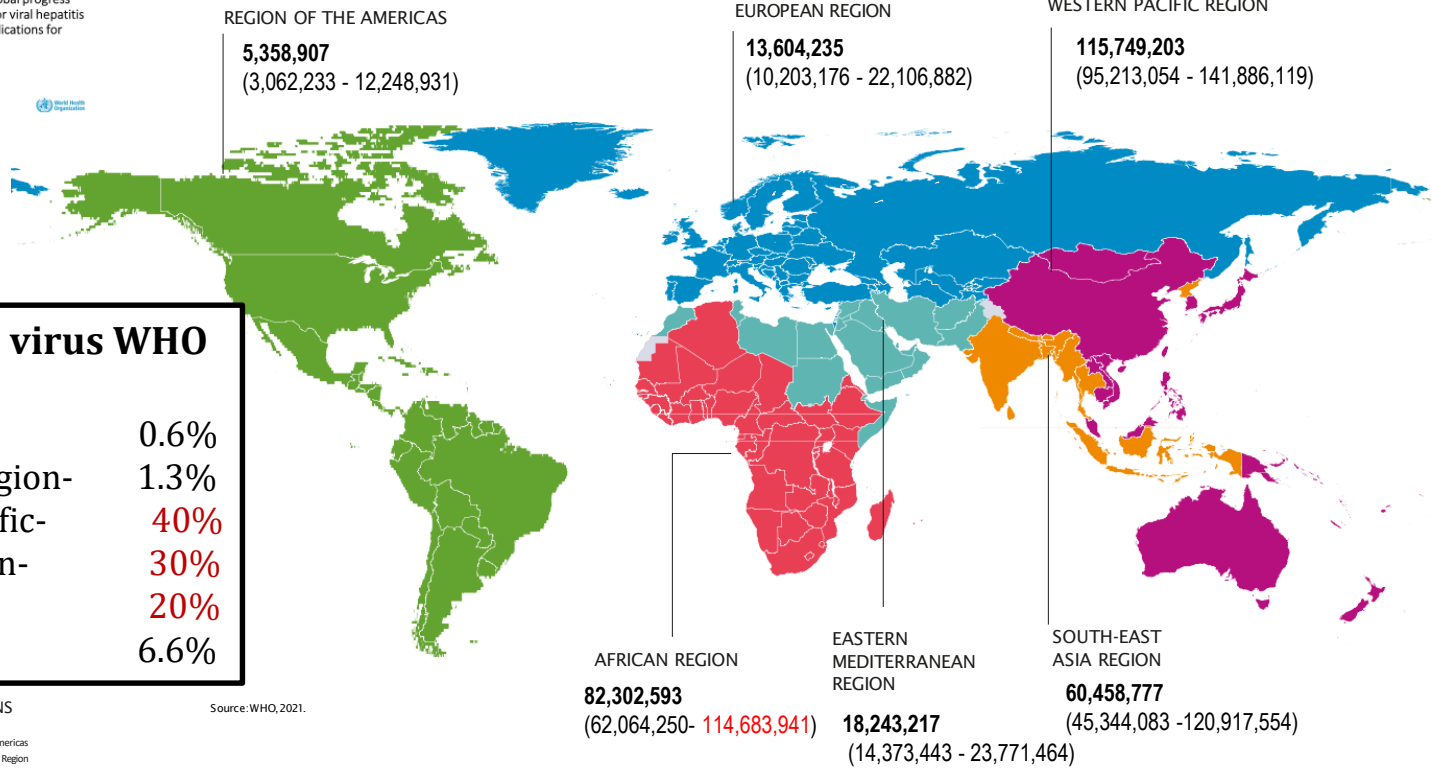
Majority of persons with HBV are unaware

< 2% of candidates are on Rx

Only about 1 in 4 adults are fully immunized

> 25% die prematurely of HCC, cirrhosis, ESLD

# Burden of Hepatitis B virus infection by WHO Region, 2019



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

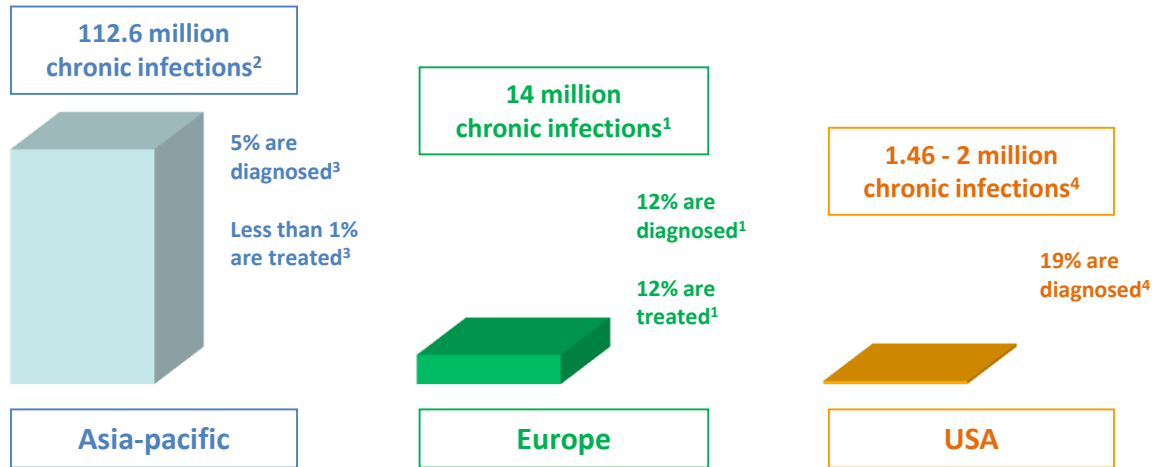
1. Hepatitis Australia. Available at [http://www.hepatitisaustralia.com/about\\_hepatitis/hep\\_b.html](http://www.hepatitisaustralia.com/about_hepatitis/hep_b.html). Accessed April 2009;

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;

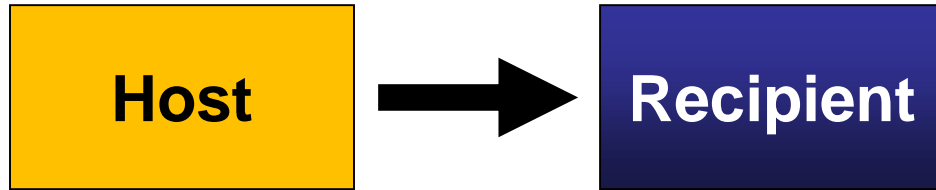
2. Mohamed R, et al. J Gastroenterol Hepatol 2004;19:958-69;

3. Decision Resources. Hepatitis B virus in China – Emerging markets study #5; 4. BMS Market Research.

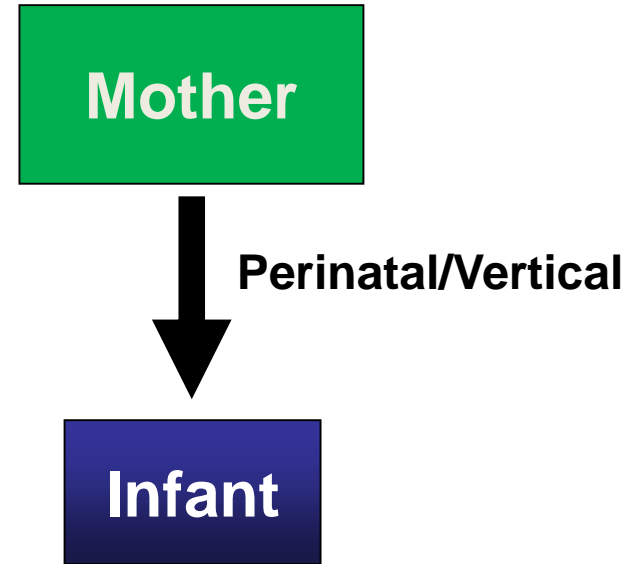


# Viral Hepatitis

## 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 Hepatitis

## CDC Screening Recommendations for HBV by Risk Factors

### Vertical transmission

Persons born in countries with 2% or higher HBV prevalence

**Pregnant women**

Infants born to HBV-infected mothers

### Blood transmission

Persons who inject drugs

Incarcerated persons

**Household contacts of HBV-infected persons**

Persons with end-stage renal disease (including hemodialysis patients)

Blood and tissue donors

### Sexual transmission

Men who have sex with men

Sexual contacts of HBV-infected persons

### HBV reactivation/liver complication

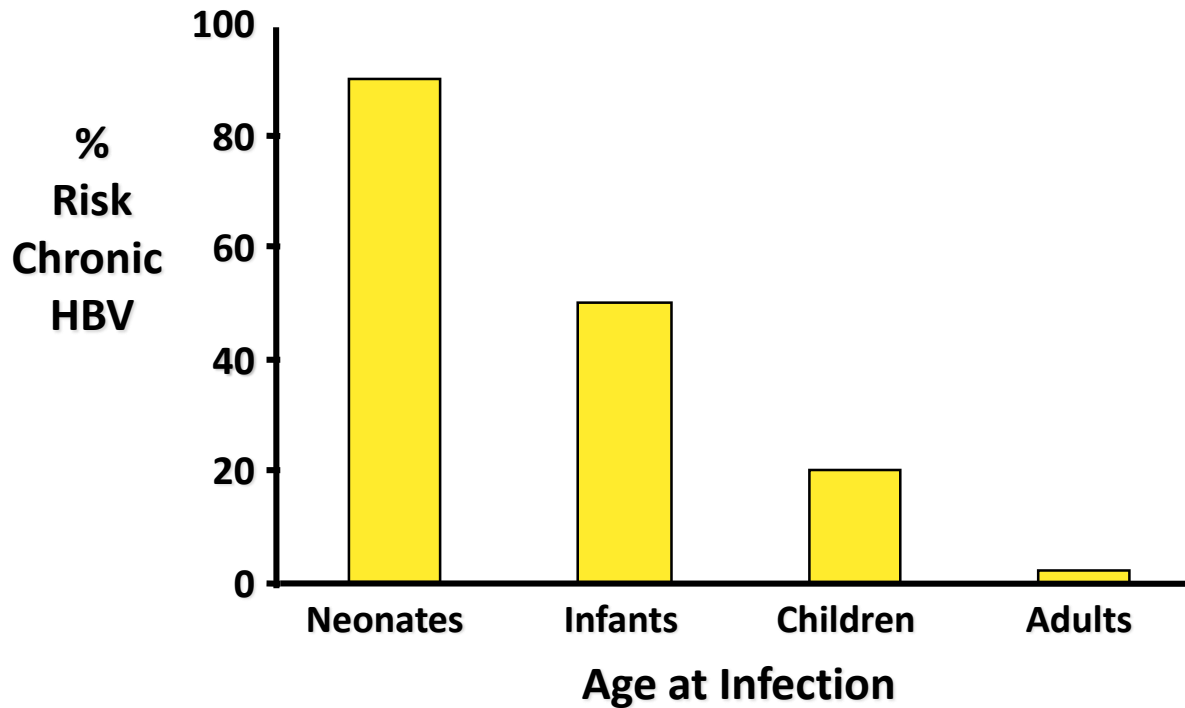
**Persons requiring immunosuppressive therapy**

Persons infected with hepatitis C virus

HIV positive persons

Persons with elevated ALT levels

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

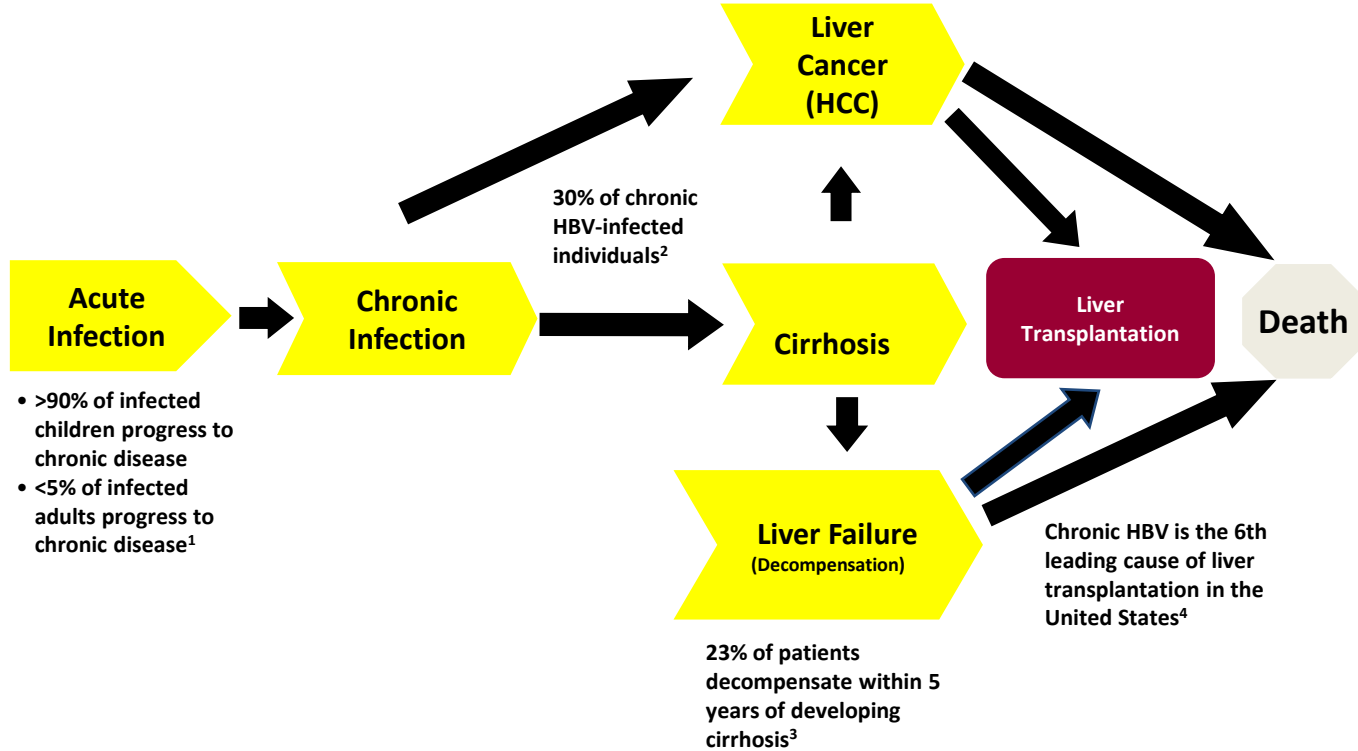


*J Infect Dis* 1985;151:599-603.

*Gastroenterology* 1987;92:1844-50.

*J Gastroenterol Hepatol* 2000;15 Suppl:E16-9.

# Hepatitis B Disease Progression



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

# 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



## 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





# 4 Phases of Chronic HBV Infection (cont.)

## 3) Inactive HBsAg carrier (non-replication)

- HBeAg negative
- Low HBV DNA (< 2,000 IU/ml)
- Normal ALT

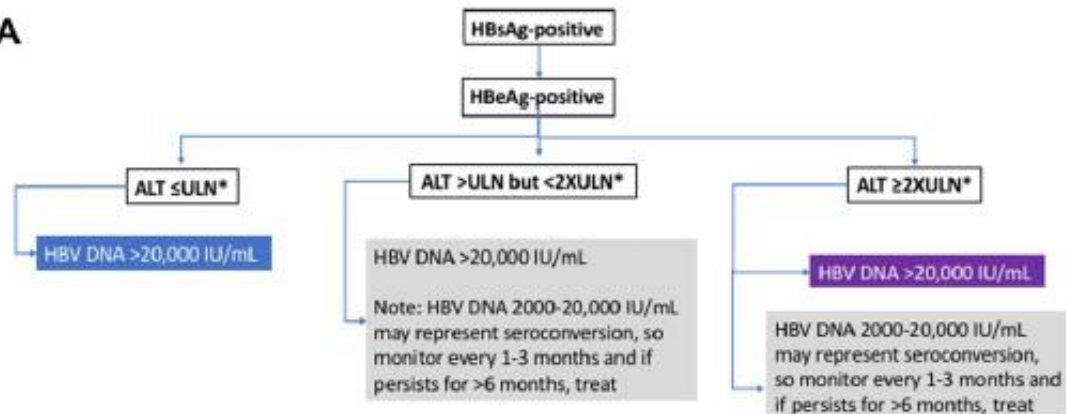


## 4) HBeAg-negative chronic hepatitis – “pre-core”

- Intermediate to high HBV DNA (> 2,000 IU/ml)
- High or fluctuating ALT
- Active inflammation on liver biopsy



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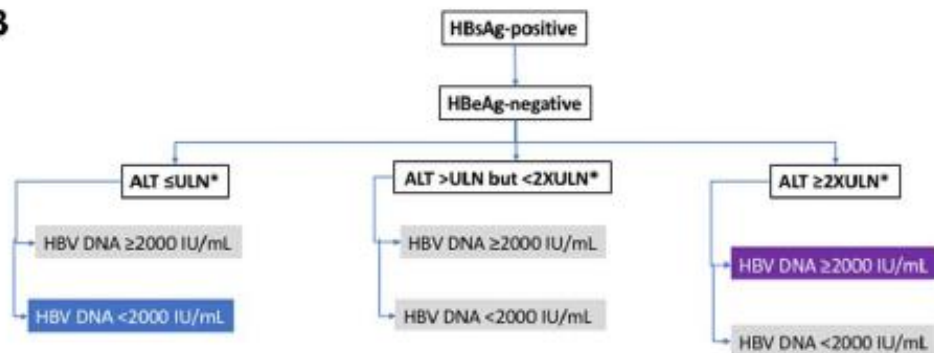


Recommendations:

**Treat**

Do not treat. Monitor with ALT and HBV DNA levels every 3-6 months and HBeAg every 6-12 months.

Exclude other causes of ALT elevation and assess disease severity with non-invasive tests and/or liver biopsy. If staging indicates ≥F2 or ≥A3, treat. If other causes of ALT >ULN excluded and elevation persists, treat, especially if age >40.

**B****Recommendations:****Treat**

Do not treat. Monitor with ALT and HBV DNA levels every 3-6 months and HBsAg annually.

If ALT  $\leq$ ULN, monitor ALT and HBV DNA every 3 months for 1 year, then every 6 months.If ALT elevated, exclude other causes of ALT elevation and assess disease severity with non-invasive tests and/or liver biopsy. If staging indicates  $\geq$ F2 or  $\geq$ A3, treat. If persistent ALT  $>$ ULN with HBV DNA  $\geq$ 2000 IU/mL, treat, especially if age  $>$ 40.

\* The upper limits of normal for ALT in healthy adults is reported to be 29 to 33 U/L for males and 19 to 25 U/L for females. An upper limit of normal for ALT of 35 U/L for males and 25 U/L for females is recommended to guide management decisions.

# 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.

# HBV Reactivation

## **Well-Characterized Syndrome**

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- 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 immunosuppression

## **Potential Consequences**

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- 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

# Viral Hepatitides

## Recommendations for Counseling for Chronic Viral Hepatitis

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- 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.