Project ECHO®

Chronic Liver Disease Foundation
New Jersey

HBV Alliance:

Expert Recommendations on Managing Patients with Chronic Hepatitis B

Accredited by

Rehoboth McKinley Christian Health Care Services

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Provided by

CLDF
Chronic Liver Disease Foundation

Hepatitis B: Update on Treatment Guidelines

Learning Objectives HBV ECHO Series

Upon completion of this activity, participants should be able to:

- Review data on the prevalence and transmission of HBV
- Define the risk of HBV among different patient populations, highlighting high-risk settings
- Describe the detrimental effects of untreated, chronic HBV to emphasize the need for diagnosis and treatment
- Demonstrate strategies to incorporate various diagnostic and treatment guidelines into clinical practice
- Analyze approved and emerging treatment options for HBV
- Identify patients that are likely to benefit from emerging treatment options versus currently available therapies

HBV Epidemiology

Countries Accounting for 80% or More of the Total HBsAg-Positive Infections in 2016

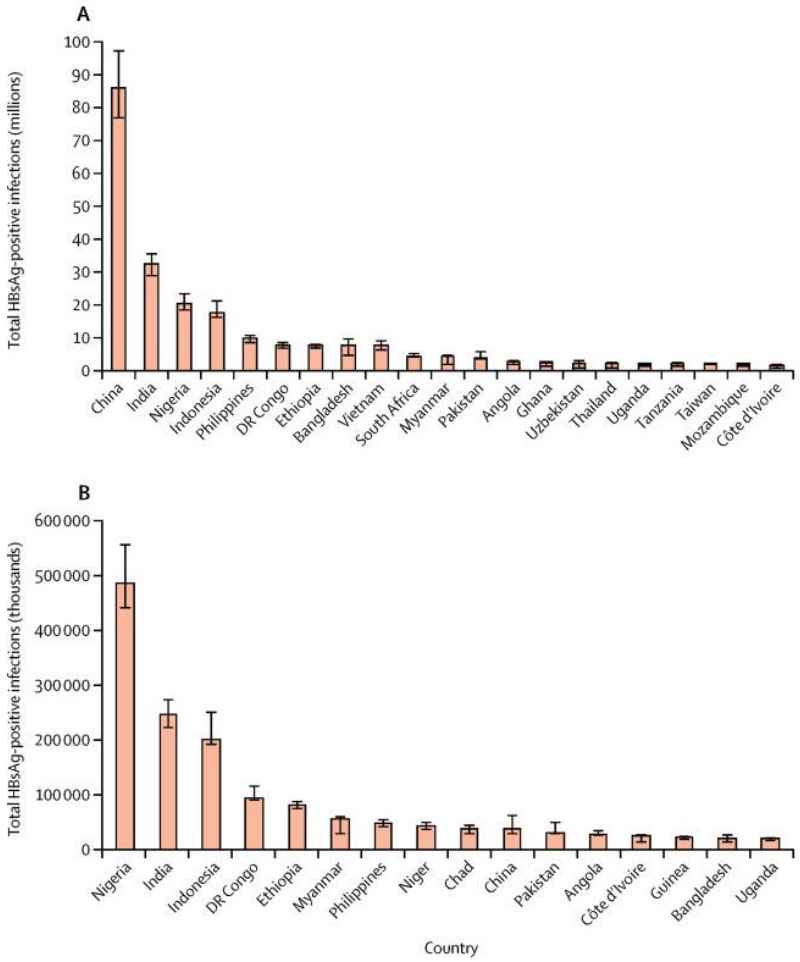


Figure 4. Countries accounting for 80% or more of the total HBsAg-positive infections in 2016
(A) General population
(B) Population aged 5 years
Polaris Observatory Collaborators. *Lancet Gastroenterol Hepatol*. 2018;3:383-403.

Prevalence of Chronic Hepatitis B Infection in the U.S.

Estimated prevalence of 1.59 million persons (range 1.25-2.49 million)

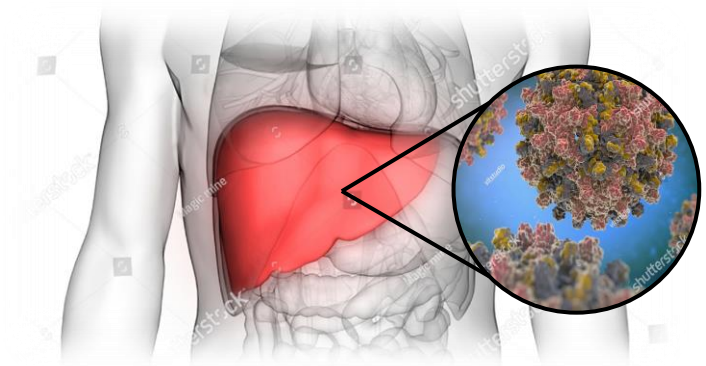
Individuals at-risk for HBV are those who are unvaccinated, fall into high-risk groups or are foreign-born and immigrating from HBV endemic regions (e.g. Asia, Africa)

Veterans
0.3 – 0.84%

Healthcare Professionals
0.1-8.1%

Prisoners
0.9-11.4%

Homeless People
0.4-1.17%



Men Who Have Sex with Men
Prevalence unknown

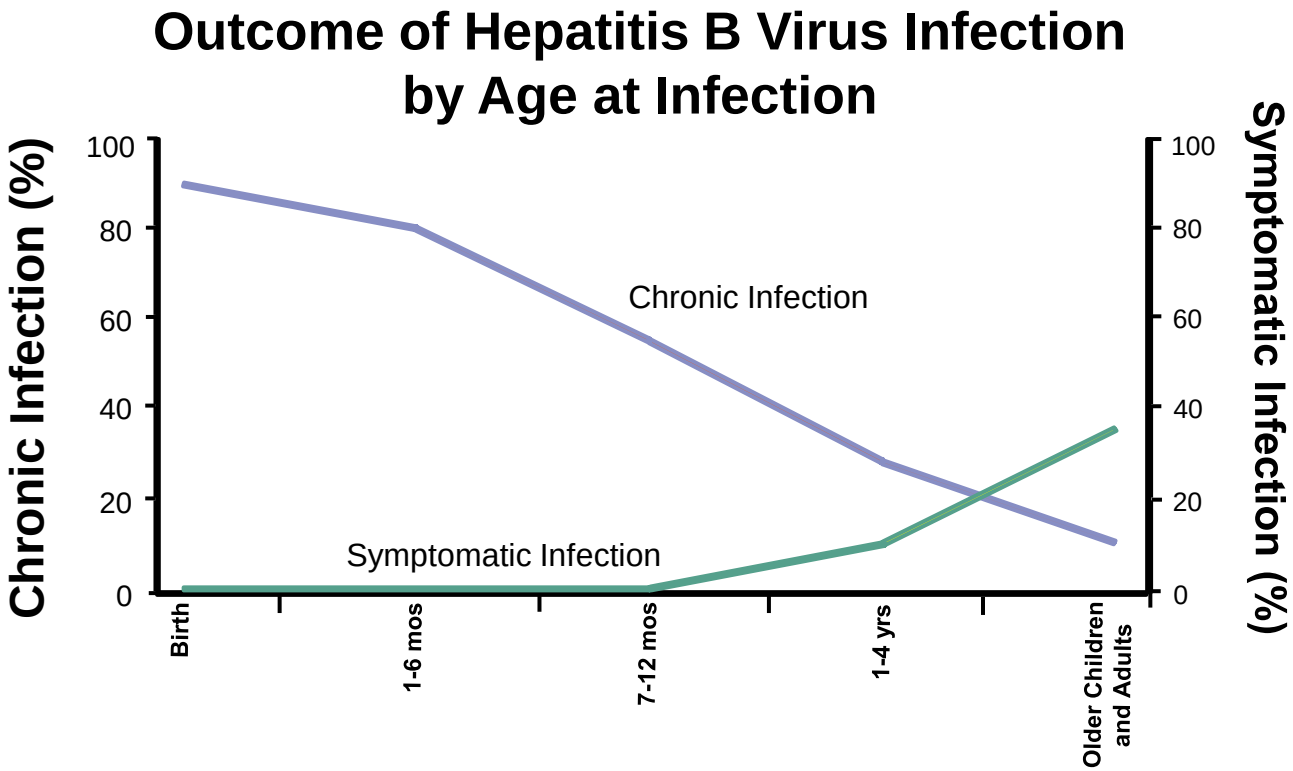
People Who Inject Drugs
11.8%

Patients with HIV Coinfection
0.7-5.8%

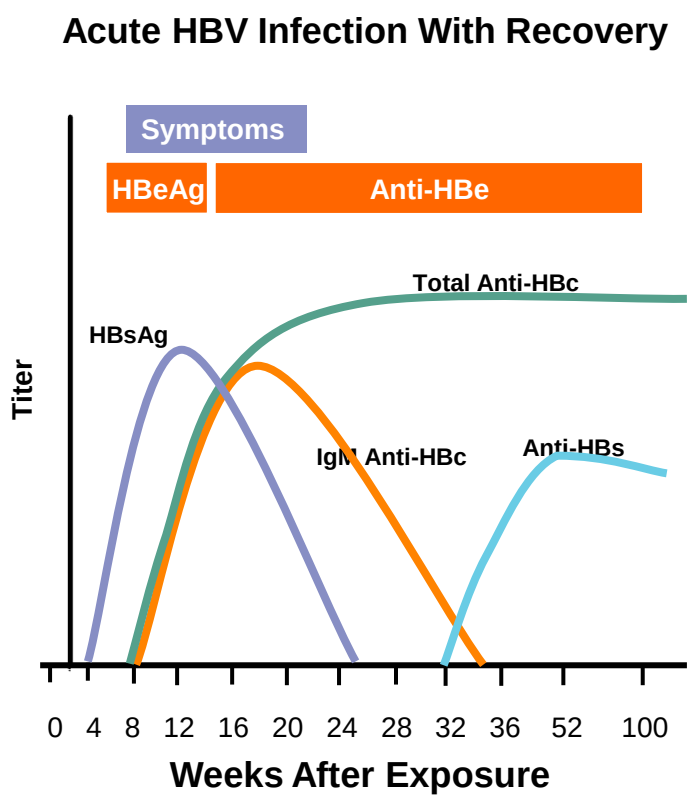
Patients HCV Coinfection
3.0-8.4%

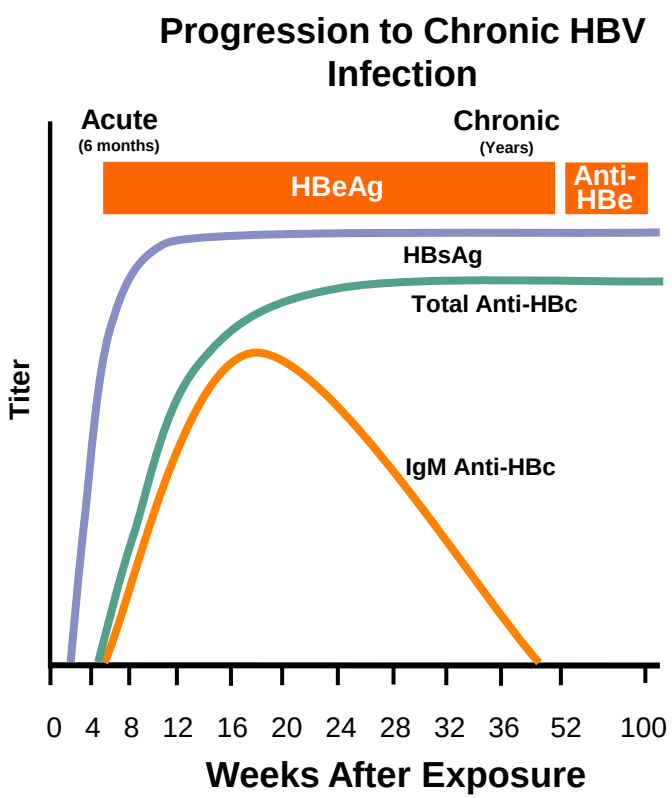
Newborns Born to HBV-Infected Mothers
3.84%

Lim J et al. *Am J Gastroenterol.* 2020, in press.


Outcome of Hepatitis B Virus Infection by Age at Infection
Chronic Infection (%)
Symptomatic Infection (%)
100
80
60
40
20
0
Chronic Infection
Symptomatic Infection
Birth
1-6 mos
7-12 mos
1-4 yrs
Older Children and Adults

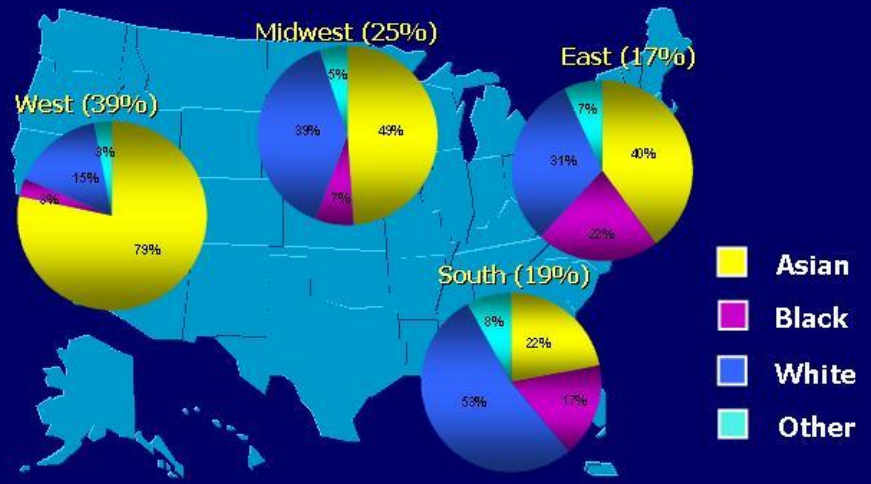
Acute and Chronic HBV Infection: Typical Serologic Course





Weinbaum CM, et al. *MMWR Recomm Rep*. 2008; 57(RR-8):1-20.

Chronicity of HBV



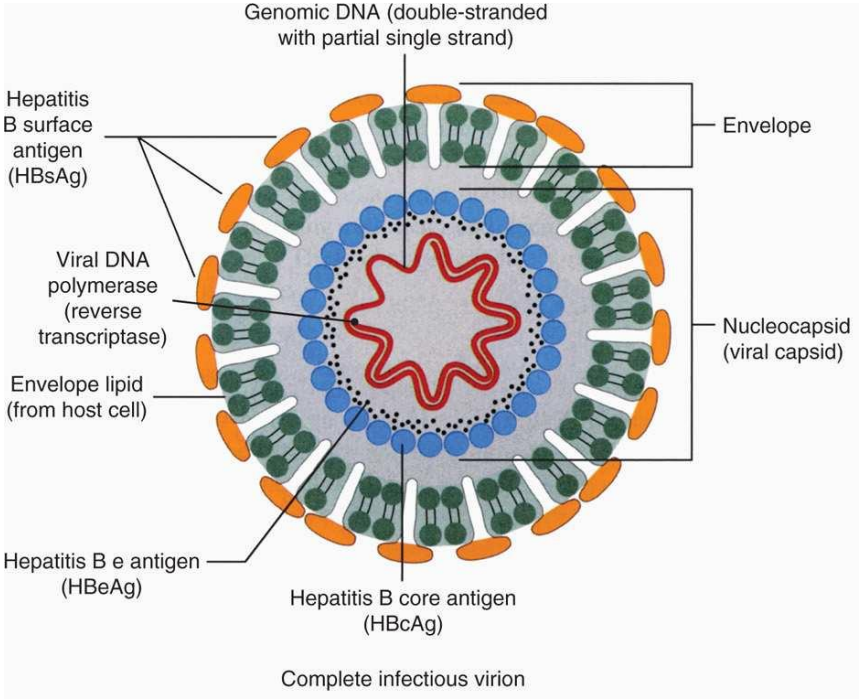
In a survey of 17 liver centers across the US, approximately 56% of HBV carriers were of Asian descent

Patient Type	Mode Transmission	Percent Developing Chronic HBV
U.S.-born	Sexual, Parenteral	2-10%
Foreign-born (Asia)	Perinatal (vertical)	80-90%

Chu. *Gastroenterology*. 2003; 125(2):444-451.

HBV Virology

HBV Structure

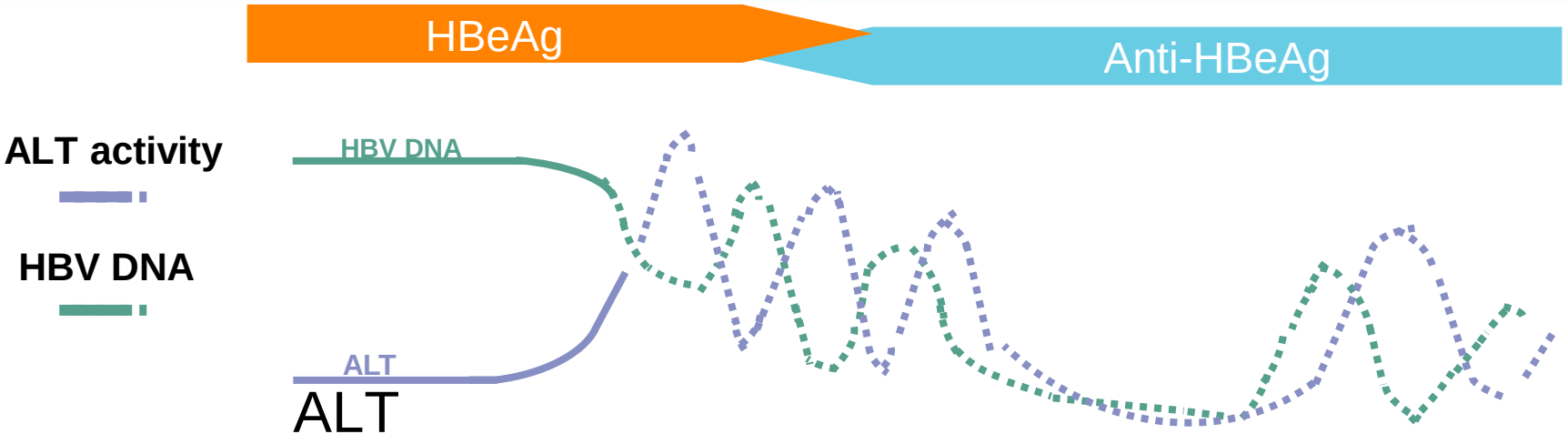


- DNA virus
- HBV replicates through an RNA intermediate and can integrate into the host genome
- Virological and serological assays have been developed for diagnosis of various forms of HBV – associated disease
- Eight genotypes, A- H

https://basicmedicalkey.com/wp-content/uploads/2017/02/image01569.jpeg
Liang JT. *Hepatology*. 2009 May; 49(5 Suppl): S13–S21.

HBV Natural History

Four Phases of Chronic HBV Infection

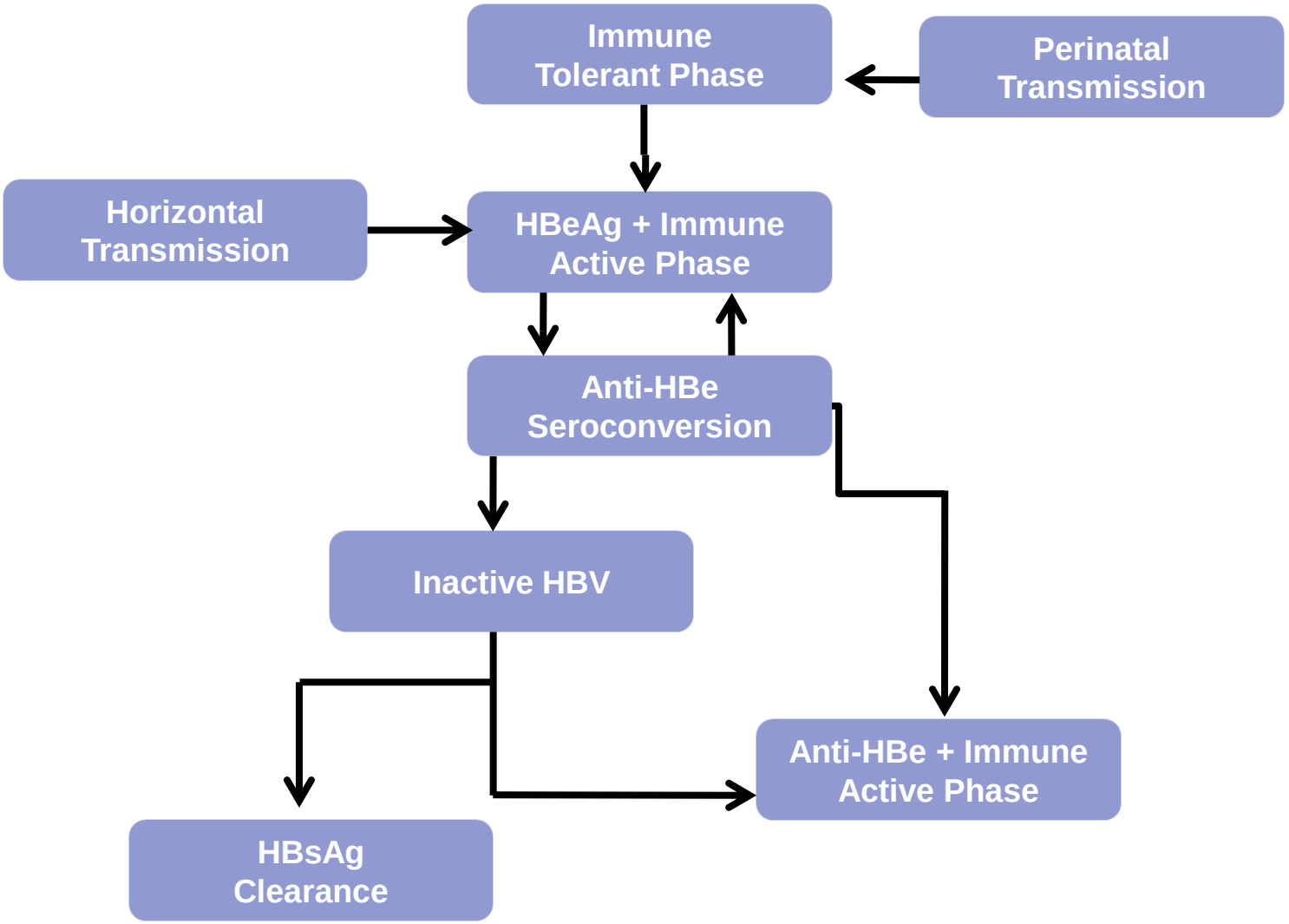


Phase	Immune Tolerant	Immune Active ("Clearance")	Inactive Carrier State (Low replication)	Reactivation
Liver	Minimal inflammation and fibrosis	Chronic active inflammation	Mild hepatitis and minimal fibrosis	Active inflammation

Optimal treatment times

Yim HJ, et al. *Hepatology.* 2006;43:S173−S181.

Natural Progression of HBV Infection



McMahon. *Clin Liver Disease*. 2010;381-396.

HBV Complications & Risk Factors

	Cirrhosis
Host	>40 years of age Male sex Immune compromised
Viral/disease	High serum HBV DNA (>2,000 IU/mL) Elevated ALT levels Prolonged time to HBeAg seroconversion Development of HBeAg-negative CHB Genotype C
Environmental	Concurrent viral infections (HCV, HIV, and HDV) Heavy alcohol use Metabolic syndrome (obesity, diabetes)

Terrault. 2016.

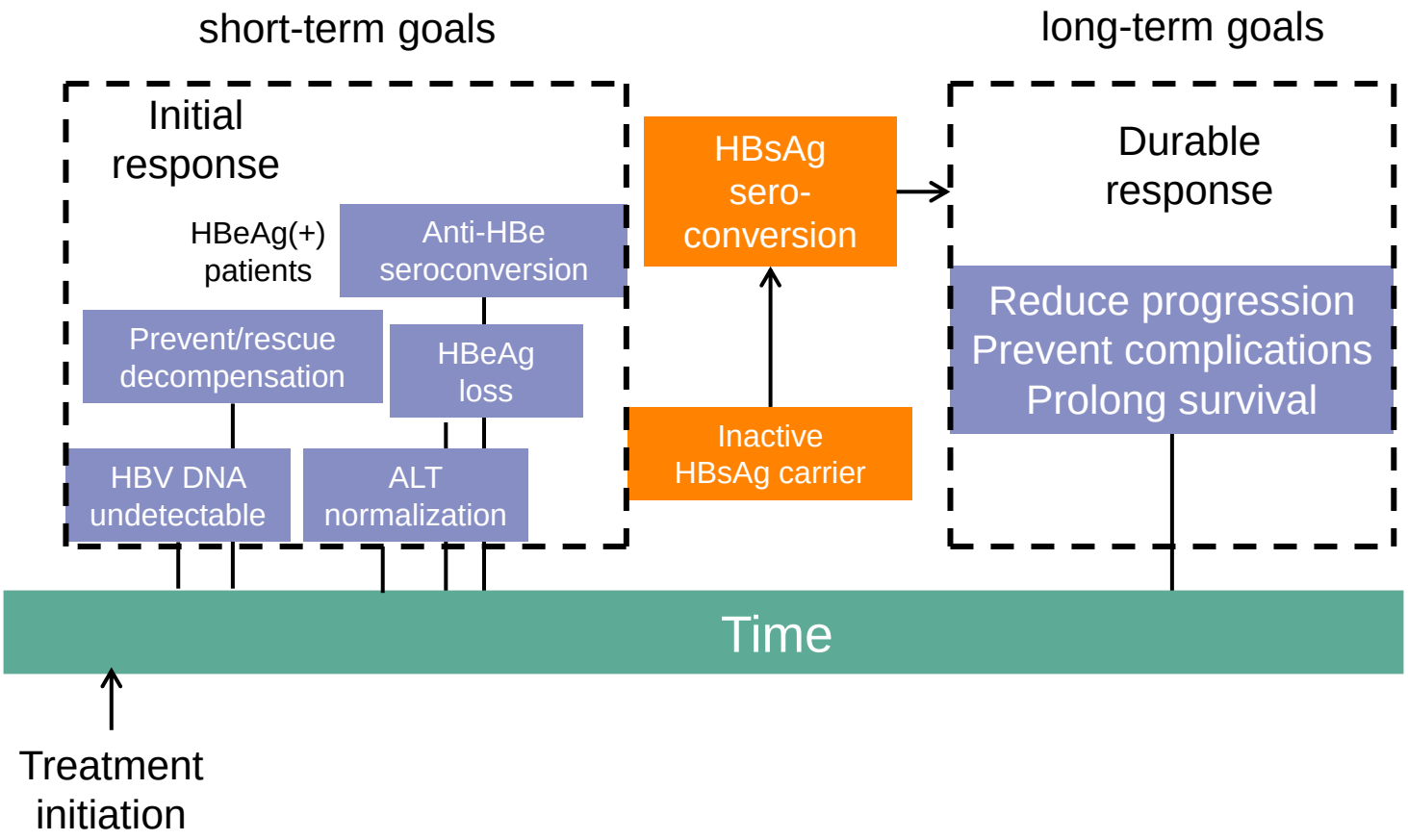
Chronic HBV: Can We Avoid Liver Biopsy

- Several studies have described use of transient elastography (Fibroscan) in chronic HBV
- Correlation with liver biopsy comparable to reports for chronic HCV
- Values ≥8.4 kPa indicate F2, ≥12.8 kPa F4
- TE now appropriate in HBV management

Afdhal. 2015.

HBV Natural Treatment

Goals of Treatment in Chronic HBV Infection



Liaw. *Clin Liver Dis*. 2013.

Approved Agents for Chronic HBV

- Lamivudine
- Adefovir
- Entecavir
- Tenofovir DF/tenofovir alafenamide
- Telbivudine
- PEG-interferon-alfa-2a

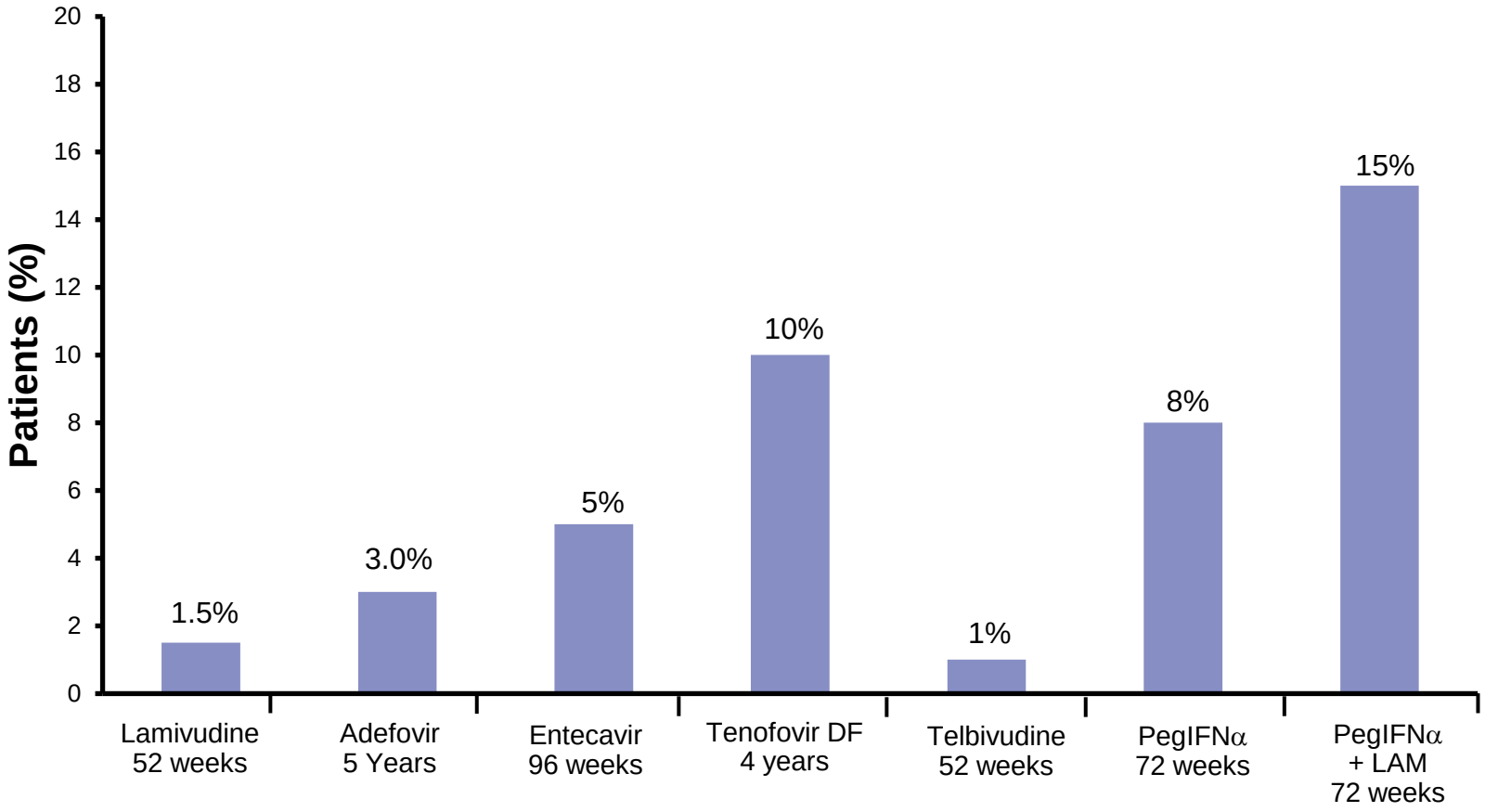
Other approved agents with anti-HBV activity

- Emtricitabine

Treatment Criteria for Chronic HBV

Guideline	HBeAg+		HBeAg-	
	HBV DNA IU/mL	ALT U/L	HBV DNA IU/mL	ALT U/L
EASL 2009	>2,000	>ULN	>2,000	>ULN
US Algorithm 2015	≥2,000	>ULN or (+) biopsy	≥2,000	>ULN or (+) biopsy
APASL 2008-12	≥20,000	>2x ULN	≥2,000	>2x ULN
AASLD	>20,000	>2x ULN or (+) biopsy	>20,000 or >2,000	≥2x ULN or (+) biopsy

HBsAg Loss in HBeAg-Positive and HBeAg-Negative Patients



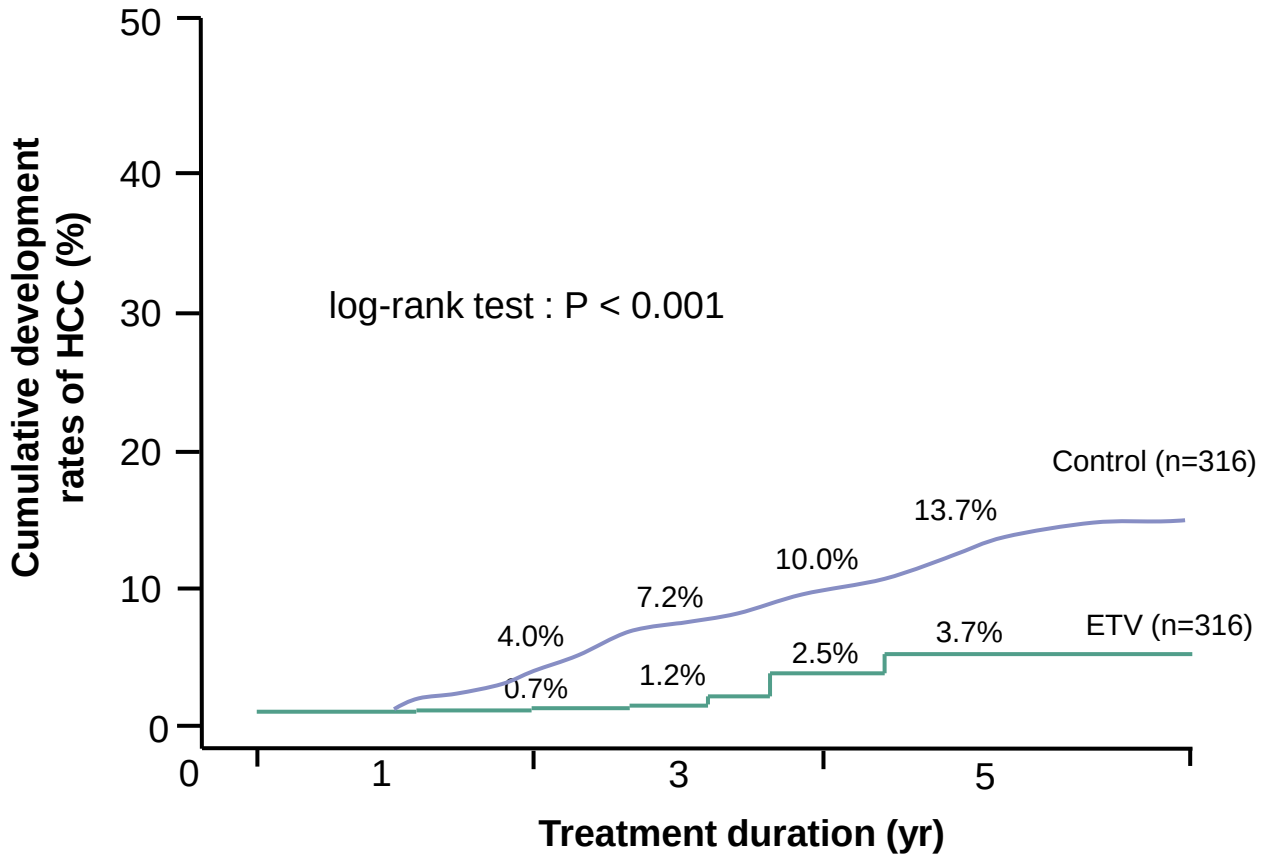
Lok AS, et al. *Hepatology*. 2009;50:661-662. Available at: http://www.aasld.org.
Heathcote EJ, et al. *Hepatology.* 2010;52(suppl):556A-557A. Abstract 477; Gish RG, et al. *J Viral Hepatitis.* 2010;17:16-22.

Reversal of Cirrhosis With TDF

- 71/96 (74%) cirrhotic patients >2 reduction in fibrosis score
- BMI ≥25 negative predictor of fibrosis regression
- 29/32 (90%) patients with normal BMI no longer cirrhotic
- HCC cumulative incidence reduced

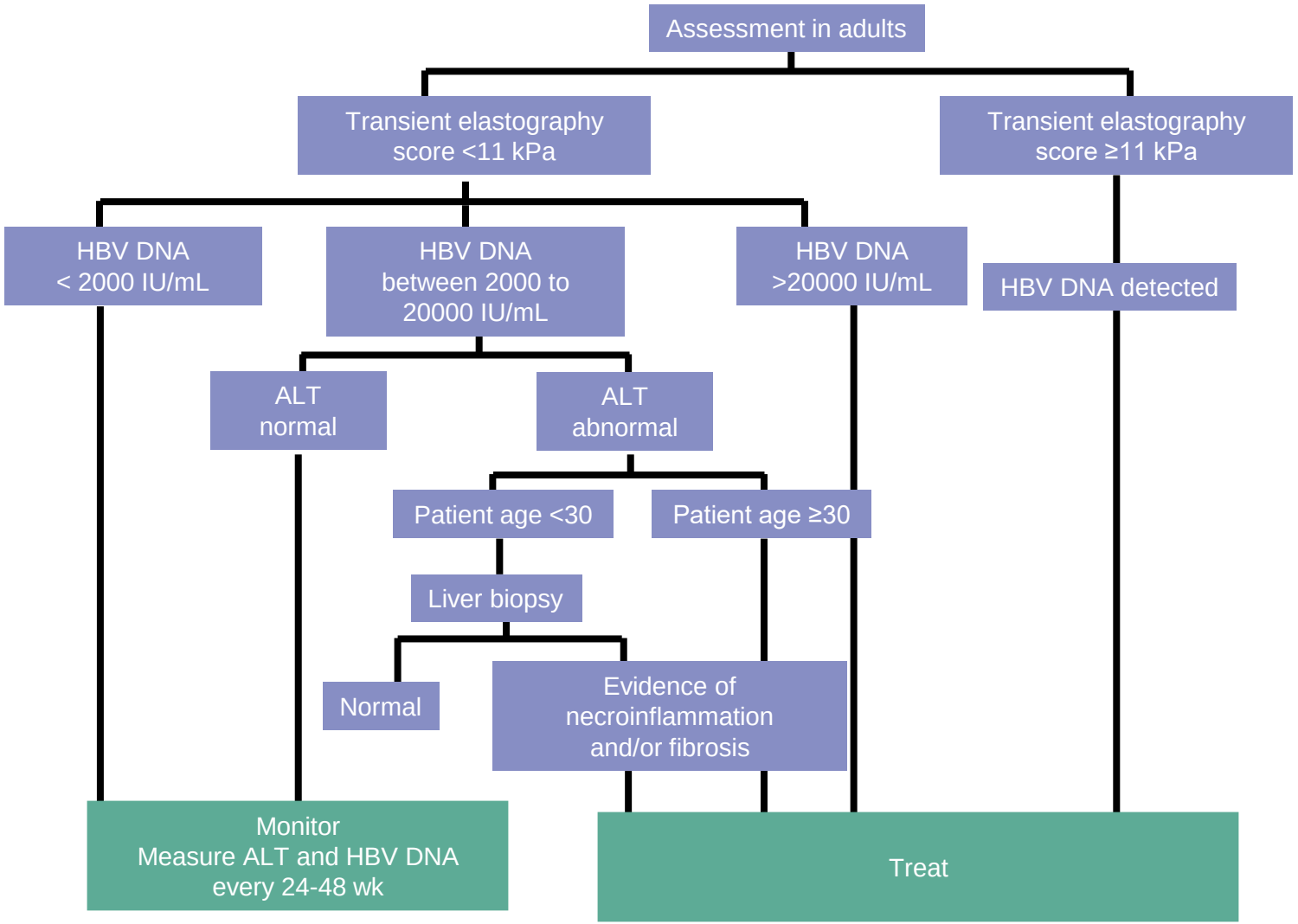
Marceliin. *Lancet*. 2013.

HCC Cumulative Incidence: Entecavir-Treated vs Nontreated Control Group After Propensity Score Matching (P <0.001)



Hosaka. *Hepatology*. 2013 Jul.

Management of Chronic Hepatitis B Infection



Tang. 2014.

How to Monitor Those Not Treated

- Liver panel monitored every 12 weeks
- HBV DNA levels every 12-24 weeks
- HBeAg/Anti-HBe for HBeAg(+) patients
- HBsAg should be tested every 6-12 months in patients who are HBeAg(-) with persistently undetectable HBV DNA by PCR
- Screen for HCC in appropriate populations

Chronic HBV: Goals of Therapy

- Achieve sustained suppression of HBV replication and remission of hepatic disease
- Prevent the development of cirrhosis, hepatic failure, and hepatocellular carcinoma
- HBV probably is never cured, but rather controlled by limiting viral replication
  - Markers of treatment response
    - Decreased serum HBV DNA to low or undetectable levels
    - Improved liver histology
    - Decreased or normalized serum ALT
    - HBeAg loss or seroconversion (in HBeAg-negative patients)
    - HBsAg loss or seroconversion

*HBV ccc DNA persists, making HBV incurable with current treatments.

Terrault NA, et al. *Hepatology*. 2016;63:261-283; Martin P, et al. *Clin Gastroenterol Hepatol.* 2015;13:2071-2087.

Thank You!