



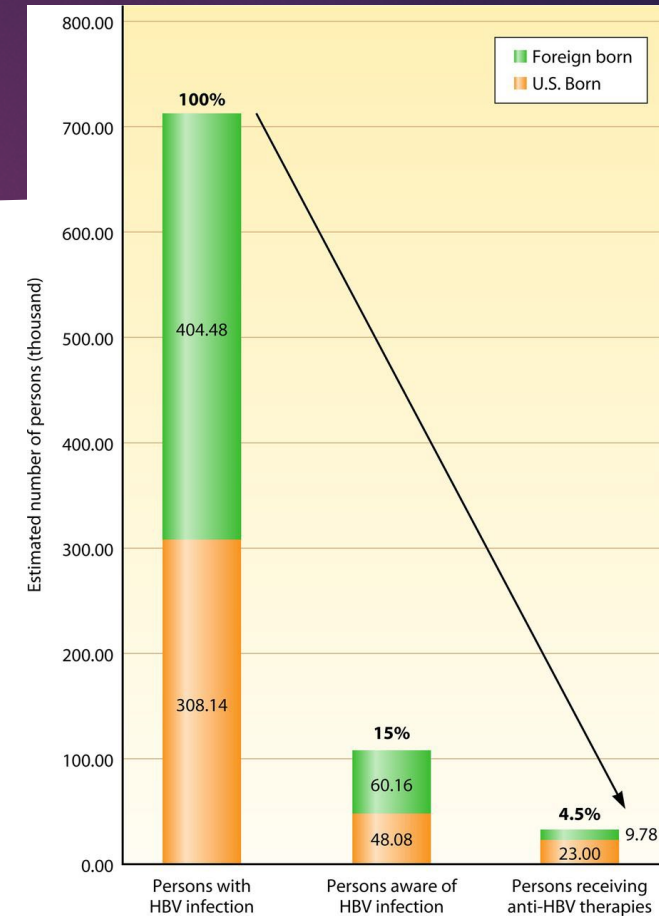
Recent Changes in Chronic Hepatitis B Treatment

BETH RUIZ, MPAS, PA-C

METHODIST TRANSPLANT INSTITUTE

Background

- ▶ HBV underdiagnosed worldwide and in the US
- ▶ Risk for cirrhosis and HCC
- ▶ Missing opportunities to start treatment to prevent disease progression
- ▶ Call to action:
 - ▶ Expand universal screening
 - ▶ Simplify current treatment guidelines



Nguyen, Mindie H., et al. "Hepatitis B virus: Advances in prevention, diagnosis, and therapy." *Clinical Microbiology Reviews*, vol. 33, no. 2, 18 Mar. 2020

Universal Screening

 Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

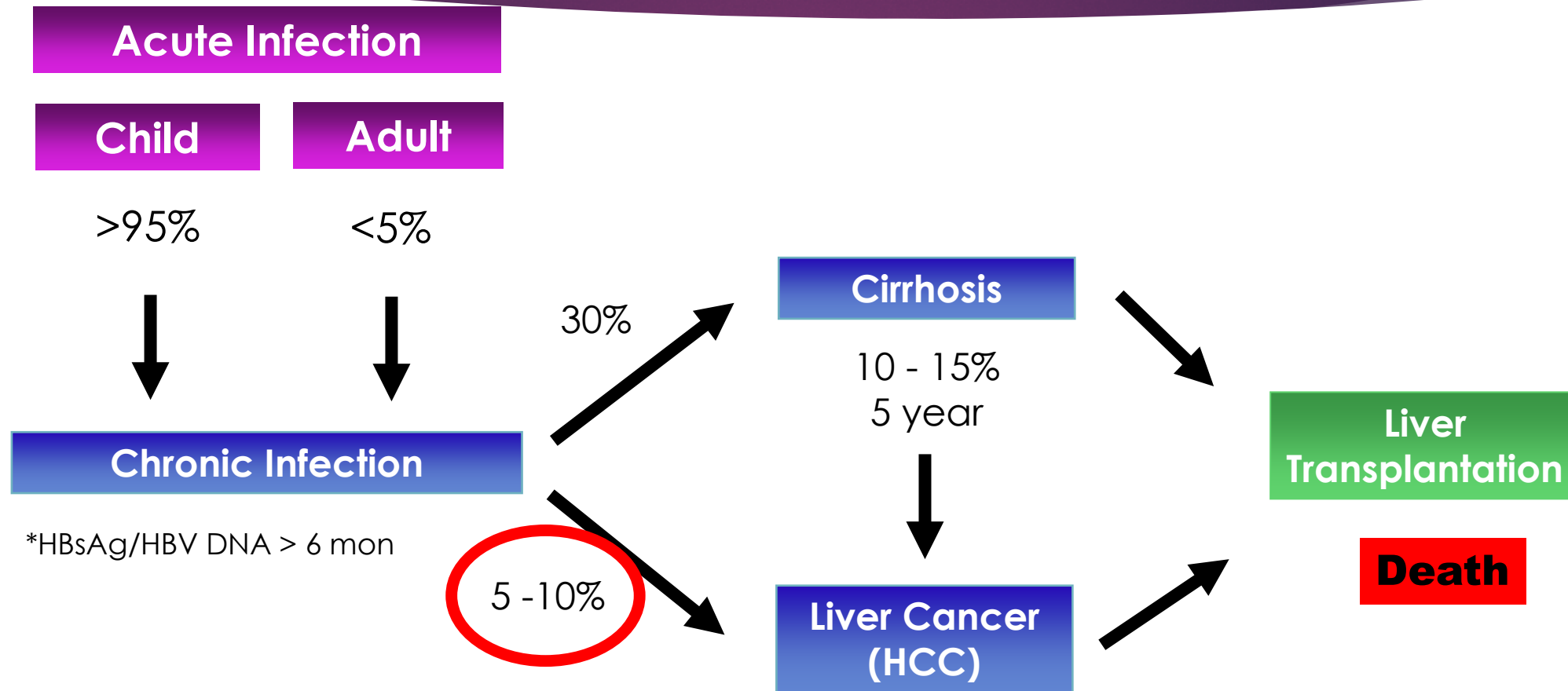
Morbidity and Mortality Weekly Report (*MMWR*)

Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations — United States, 2023

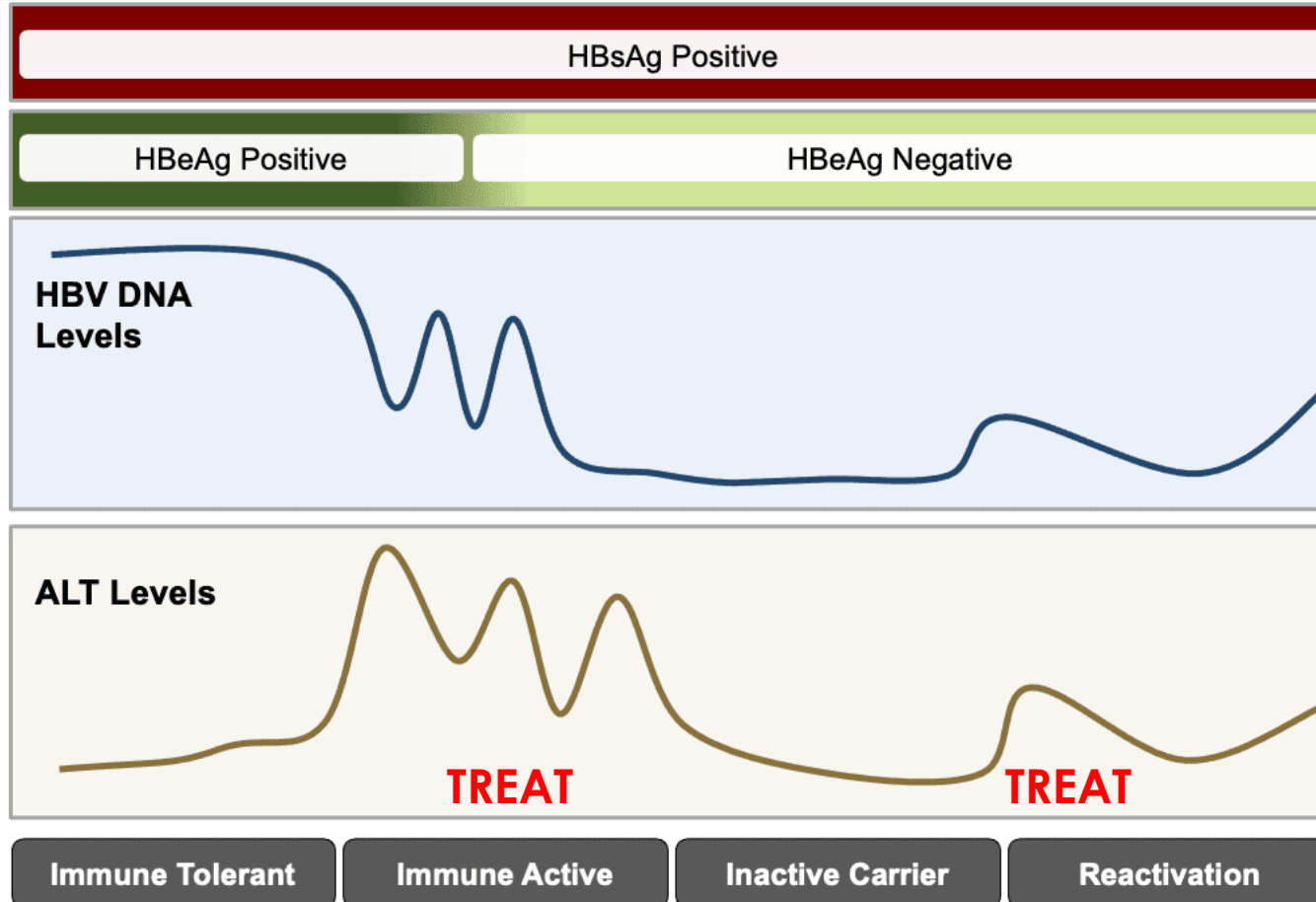
Recommendations and Reports / March 10, 2023 / 72(1);1–25

- ▶ Updated CDC Recommendations for all adults > 18 years of age
 - ▶ Hepatitis B surface antigen
 - ▶ Hepatitis B surface antibody
 - ▶ **Total hepatitis B core antibody added**
 - ▶ Potential risk of HBV reactivation with biologic therapies

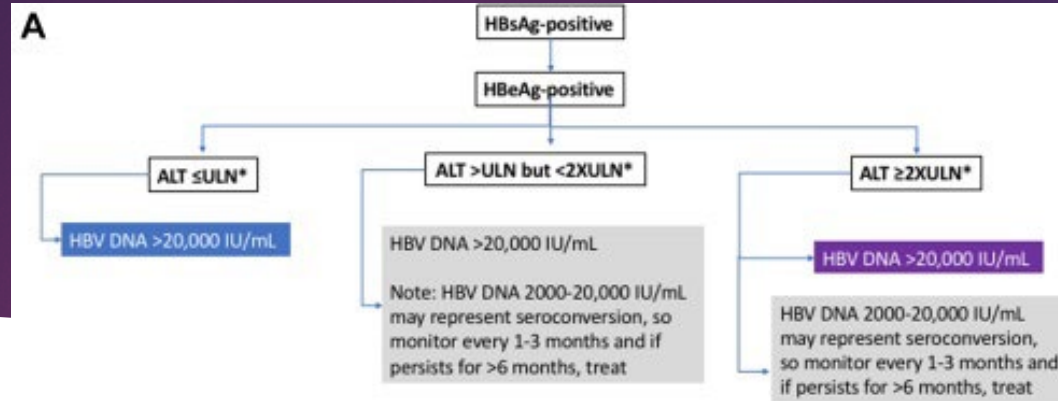
Hepatitis B Disease Progression



Immune Phases



≥ F2 TREAT

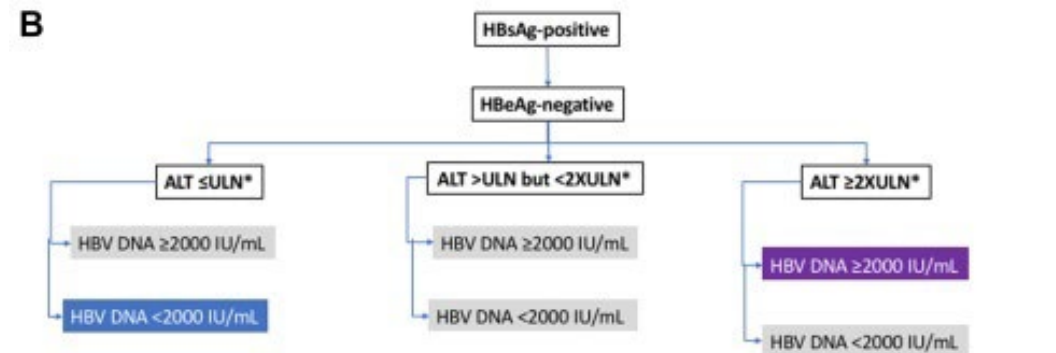


Recommendations:

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 \geq F2 or \geq A3, treat. If other causes of ALT >ULN excluded and elevation persists, treat, especially if age >40.



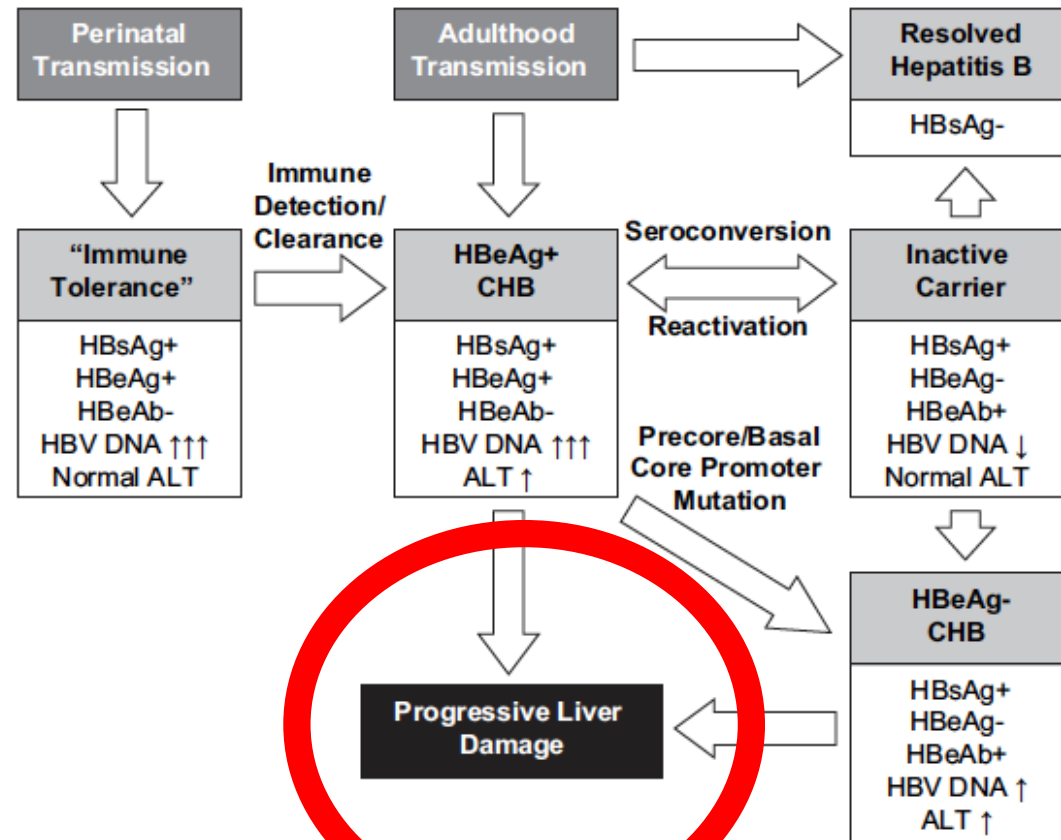
Recommendations:

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 39 U/L for males and 25 U/L for females is recommended to guide management decisions.



Courtesy of WR Kim MD, Mayo Clinic, Rochester Minnesota

Fig. 1. Classic phases in chronic HBV infection. (Courtesy of W.R. Kim, MD, Rochester MN.)

AGA Simplified Chronic HBV Treatment Guidelines

Gastro Hep Advances 2023;2:209–218

- ▶ Fibrosis testing \geq F2
- ▶ No Fibrosis:

ORIGINAL RESEARCH—CLINICAL

It Is Time for a Simplified Approach to Hepatitis B Elimination

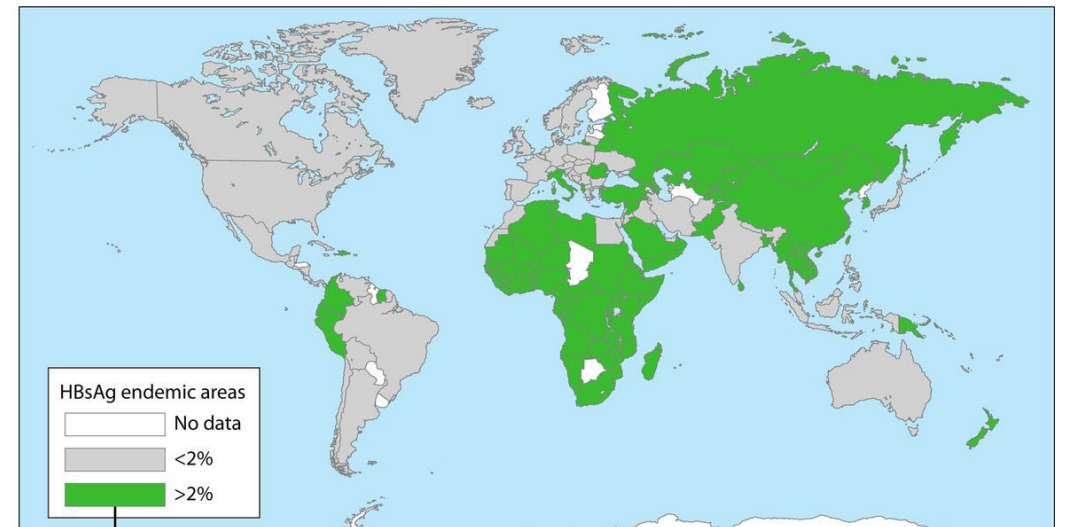
Douglas Dieterich,¹ Camilla Graham,² Su Wang,³ Paul Kwo,⁴ Young-Suk Lim,⁵ Chun-Jen Liu,⁶ Kosh Agarwal,⁷ and Mark Sulkowski⁸



Age	HBV DNA	ALT
< 30 years	>2000 IU/mL	>ULN (30 IU/mL men, 19 IU/mL women)
>30 years	>2000 IU/mL	*Regardless of ALT levels

Additional Factors to Consider

- ▶ Age >40 years
- ▶ Endemic areas
- ▶ FH cirrhosis or HCC
- ▶ Previous treatment (peg-IFN, NA exposure)
- ▶ Extrahepatic manifestations
 - ▶ Polyarteritis nodosa
 - ▶ Glomerulonephritis

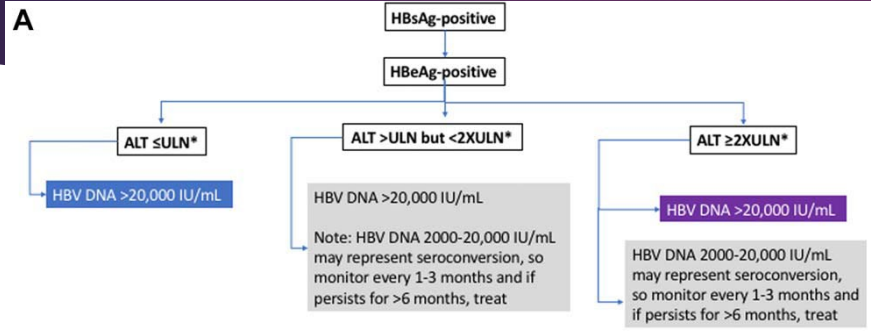


Nguyen, Mindie H., et al. "Hepatitis B virus: Advances in prevention, diagnosis, and therapy." *Clinical Microbiology Reviews*, vol. 33, no. 2, 18 Mar. 2020

Case

- ▶ 50 year old African American female
 - ▶ Diagnosed chronic hepatitis B over 20 years ago, treatment naive
 - ▶ HBsAg positive
 - ▶ HBV DNA 2,341 IU/mL
 - ▶ ALT 13
 - ▶ FIB4 0.82 low risk fibrosis
- ▶ Should this patient be started on anti-viral treatment?
- ▶ **YES!**

Case

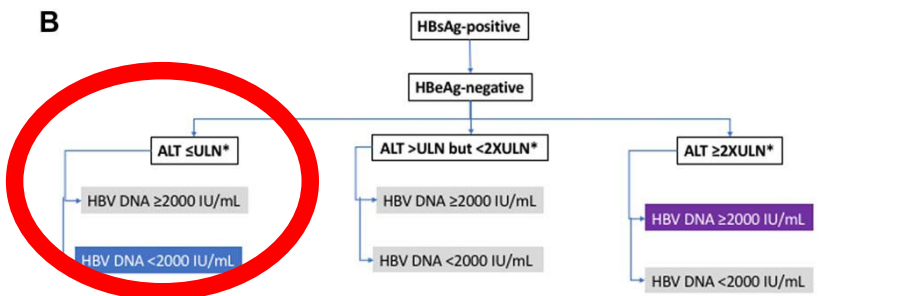


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Recommendations:

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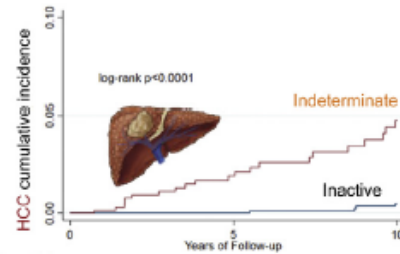
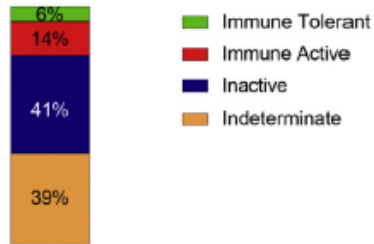
Age	HBV DNA
>30 years	>2000 IU/mL

Indeterminate Phase HCC Risk

Natural History and HCC Risk in Chronic Hepatitis B Indeterminate Phase

3,366 treatment naïve CHB patients

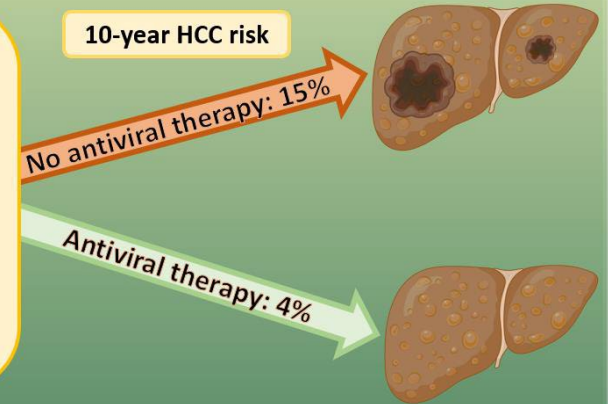
- ✓ 39% were in the **indeterminate** phase at baseline
- ✓ **HCC** risk among **indeterminate** patients was 14X that of inactive patients



Huang et al. Distribution of clinical phases (%) at baseline

Clinical Gastroenterology and Hepatology

- 855 patients with chronic hepatitis B persistently in the *indeterminate phase* (not meeting standard criteria for immune-tolerant, immune-active, or inactive)
- 14 centers from U.S., Europe, and Asia (REAL-B Consortium)
- Baseline characteristics balanced by inverse probability of treatment weighting



Huang D/Nguyen MD et al, *Hepatology* 2023; 78(5):1558-1568

- ▶ Conclusion antiviral treatment reduces HCC risk by 70% indeterminate phase patients

Nucleoside Analogues

Goals of treatment - reduce HBV DNA to undetectable levels, normalize ALT, and reduce inflammation and fibrosis

Entecavir 0.5mg daily

- ▶ Increase dose 1mg for decompensated cirrhosis
- ▶ Avoid with previous lamivudine resistance

Tenofovir disoproxil fumarate (TDF) 300mg daily

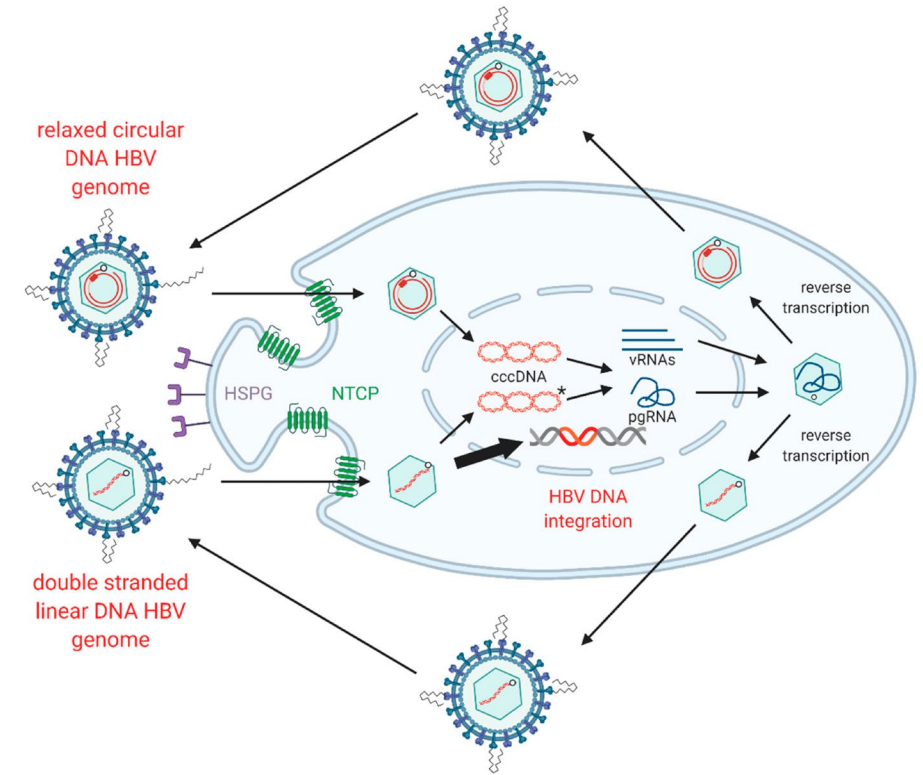
- ▶ Treatment for pregnant women 3rd trimester HBV DNA >200,000 to prevent perinatal transmission
- ▶ Concerns for increased renal toxicity and BMD loss (switch to entecavir or TAF)

Tenofovir alafenamide (TAF) 25mg daily

- ▶ Prior treatment or antiviral resistance
- ▶ HIV/HBV
- ▶ Less systemic exposure, decreased renal and bone toxicity concerns

Search for a HBV Cure

- ▶ Unable to eradicate virus
- ▶ Persistence covalently closed circular DNA (cccDNA) in nucleus of infected hepatocytes
- ▶ HBV genome integrates into the host DNA
 - ▶ Promotes oncogenesis and increased risk HCC



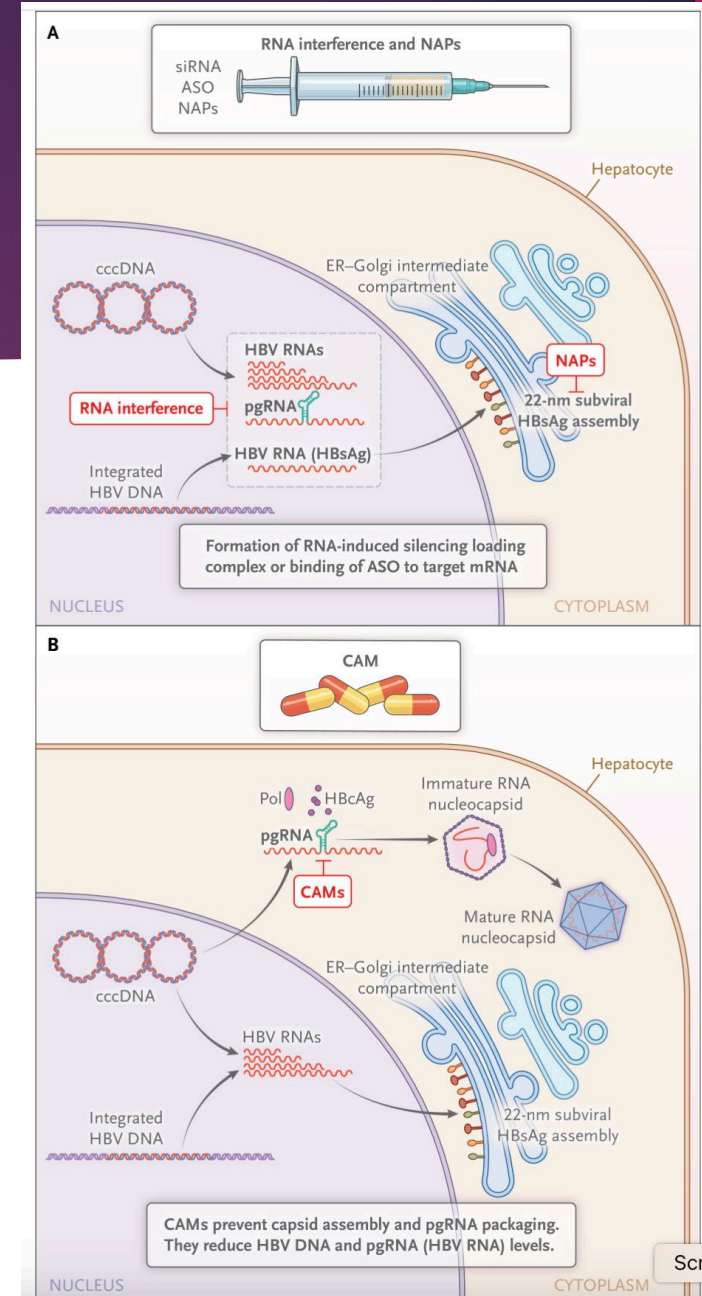
REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

New Approaches to Chronic Hepatitis B

Geoffrey Dusheiko, M.D., Kosh Agarwal, M.D., and Mala K. Maini, M.D., Ph.D.

- ▶ Investigational therapies
 - ▶ **RNA interference agents** – target mRNA to suppress HBsAg production from both cccDNA and integrated HBV DNA
 - ▶ **Nucleic acid polymers (NAPs)** - inhibit HBsAg assembly
 - ▶ **Capsid assembly modulators (CAMs)** - prevent capsid assembly and decrease both HBV DNA and RNA levels
 - ▶ **Entry Inhibitors**
 - ▶ **Immunotherapy**



Take Home Points

- ▶ **Universal screening** expanded all adults and includes total hepatitis B core antibody
- ▶ **Proposed chronic HBV simplified treatment**
 - ▶ Fibrosis testing **>F2 TREAT**
 - ▶ If no Fibrosis **TREAT** for:

Age	HBV DNA	ALT
< 30 years	>2000 IU/mL	>ULN (30 IU/mL men, 19 IU/mL women)
>30 years	>2000 IU/mL	*Regardless of ALT

- ▶ Preferred treatments TAF 25mg and Entecavir
- ▶ **HCC screening with imaging (US or contrast CT/MRI) with AFP every 6 months**

Thank you!