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HEPATITIS

Key Slides on Hepatitis B Pretreatment Evaluation

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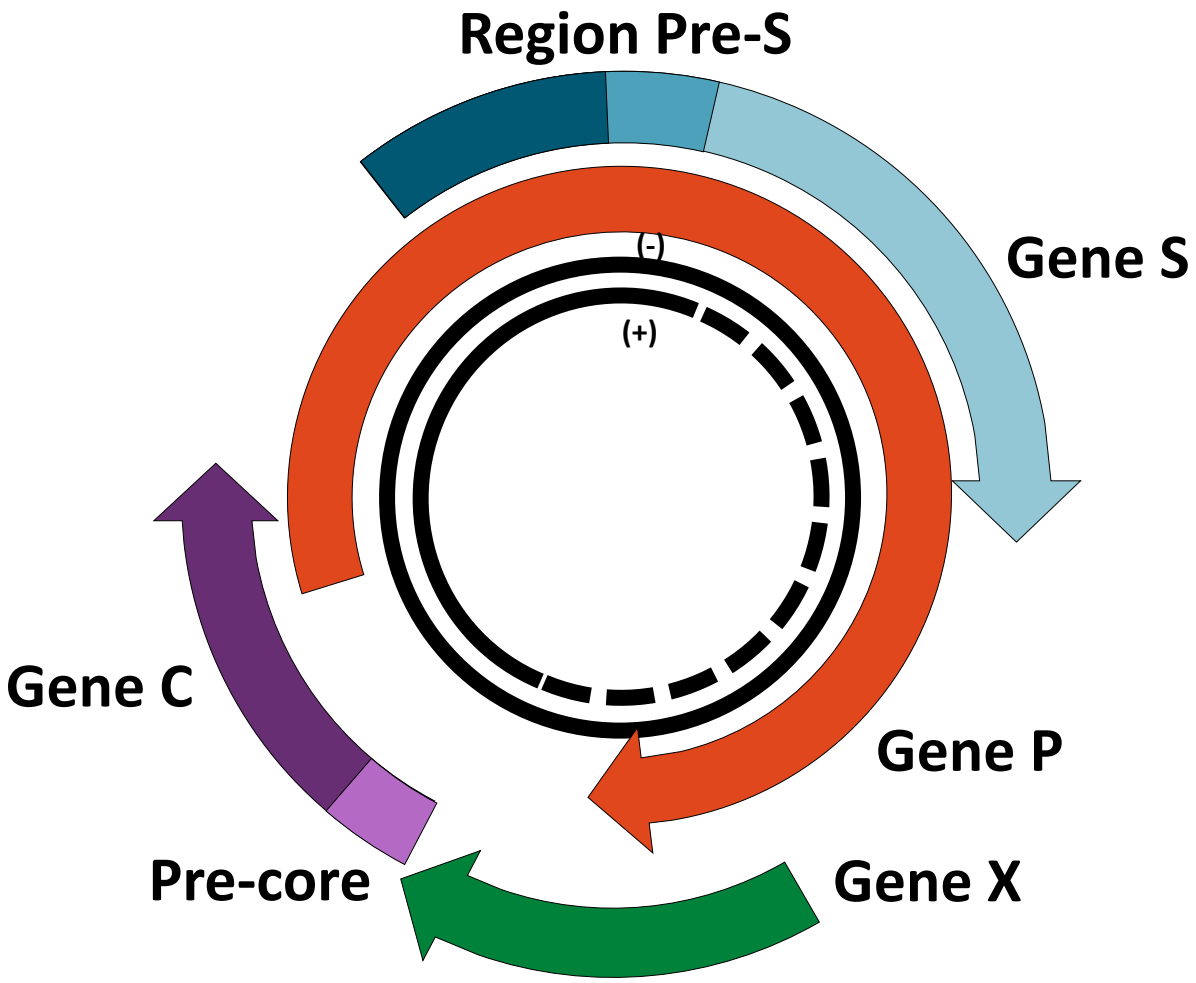
Hepatitis B Gene Products



Products
- HBsAg
- DNA polymerase
- HBxAg
- HBcAg/HBeAg

Alexopoulou. J Clin Med. 2020;9:3187.

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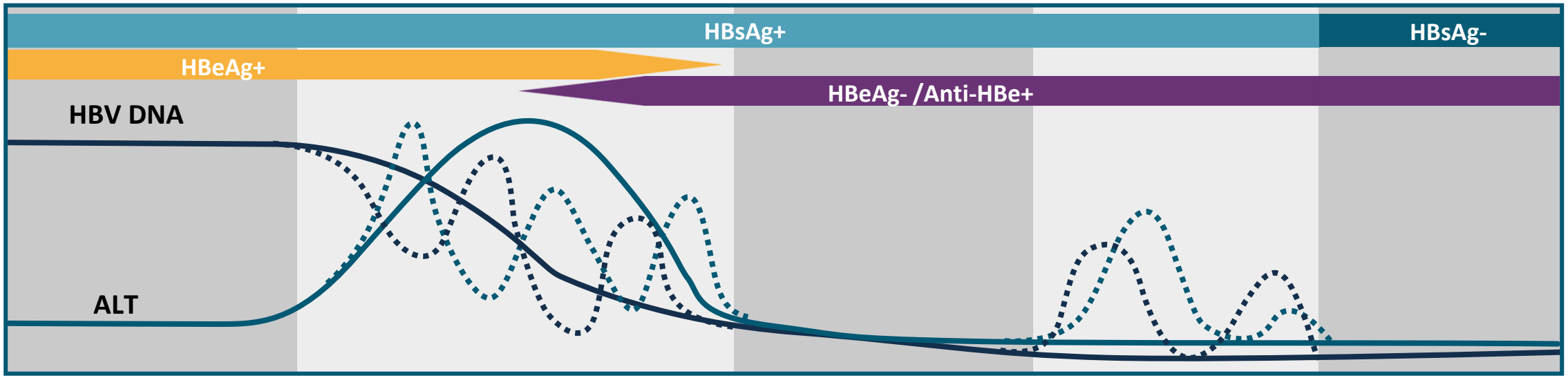
Hepatitis B Serology

Serum Test[1,2]	Description	Positive Result Interpretation	Additional Considerations
Anti-HBc IgM	IgM antibody to HBV core antigen	Indicates recent infection (≤ 6 mos)	Occasionally occurs in presence of severe flare of chronic HBV disease
HBsAg	HBV surface antigen	Indicates an individual is infected or infectious	Can be detected during acute or chronic infection
Anti-HBs	Antibody to HBV surface antigen	Indicates recovery and immunity	Also develops following vaccination against HBV
Anti-HBc	Antibody to HBV core antigen	Indicates exposure (previous or ongoing)	Appears at the onset of symptoms in acute infection and persists for life
HBeAg	HBV e antigen	Indicates presence of actively replicating virus, high levels of HBV DNA, and high transmissibility	Detectable during acute and chronic infection
Anti-HBe	Antibody to HBV e antigen	Seroconversion from e antigen to e antibody predicts emergence of precore or core promoter mutant infection and transition to chronic HBeAg-negative disease in persons not on treatment or long-term clearance of HBV in patients on treatment	Detectable transiently during acute infection or consistently during or after a burst in viral replication in the setting of wild-type infection clearance

1. https://www.cdc.gov/hepatitis/hbv/pdfs/SerologicChartv8.pdf 2. Kamijo. World J Gastroenterol. 2015;21:541.

Course of HBV Infection



- Patients with perinatally acquired infection
- Minimal/no inflammation
- May last 1-4 decades
- **EASL: chronic infection[3]**

- High or fluctuating HBV DNA
- Persistent or intermittent fluctuation in ALT
- Active inflammation and liver damage
- **EASL: chronic hepatitis[3]**

- Low/undetectable HBV DNA
- Normal ALT
- Mild hepatitis/minimal fibrosis, but cirrhosis may be present from previous liver damage
- **EASL: chronic infection[3]**

- Usually older patients with more advanced liver disease
- Fluctuating levels of ALT and HBV DNA
- **EASL: chronic hepatitis[3]**

- After many years of infection in some patients
- Not considered a "cure" because intracellular HBV DNA is still present

CHB follows a nonlinear clinical course; not all patients will go through each phase.

1. Tong. Dig Dis Sci. 2011;56:3143. 2. Yim. Hepatology. 2006;43:S173. 3. EASL. J Hepatol. 2017;67:370.

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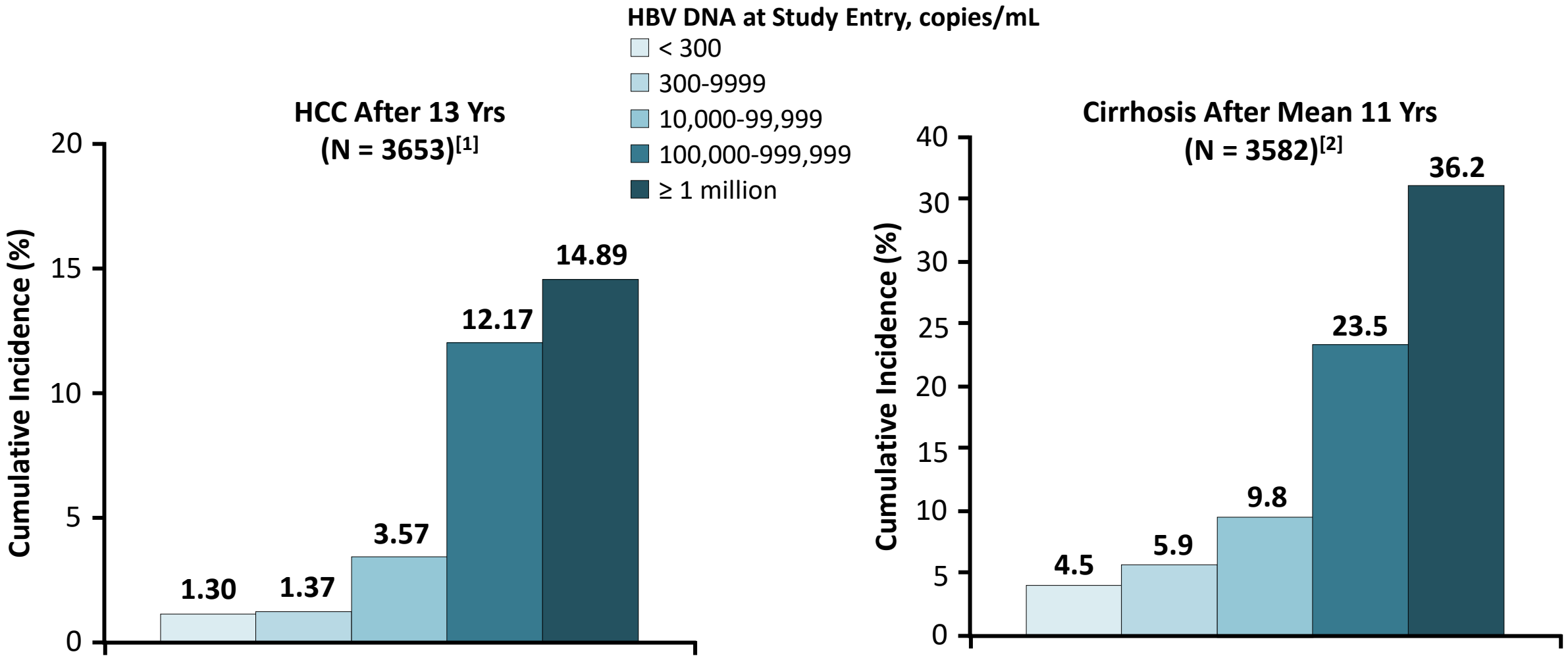
REVEAL-HBV: HBV DNA Levels and Long-term Outcomes



1. Chen. JAMA. 2006;295:65. 2. Iloeje. Gastroenterology. 2006;130:678.

Slide credit: clinicaloptions.com

Pretreatment Evaluation for Hepatitis B

Pretreatment Tests
Serial ALT and HBV DNA for 6 mos
LFTs: CBC, hepatic function panel, prothrombin time
HBeAg and anti-HBe
HBV genotype
Tests to rule out other causes of liver disease: anti–hepatitis C virus, anti–hepatitis D virus
Hepatitis A immunity: anti–hepatitis A virus IgG or total
HIV: anti-HIV
Screen for HCC in high-risk patients: ultrasound and AFP
Transient elastography to grade histologic fibrosis or liver biopsy examination to grade and stage liver disease
Urinalysis: if abnormal, 24-hr urine for creatinine and protein

History and Physical Examination
Risk factors for viral hepatitis
Duration of infection
Route of transmission
Risk factors for HIV coinfection
Alcohol history
Presence of comorbid diseases
Family history of liver cancer
HBV testing of family members
General counseling on transmission
Vaccination of at-risk household contacts
Family planning

Martin. Clin Gastroenterol Hepatol. 2015;13:2071.

Defining Normal Liver Chemistry Tests

ALT ULN	AASLD 2018[1]	EASL 2017[2]
Males	35 U/L	40 IU/L
Females	25 U/L	40 IU/L

- Normal ALT levels in prospectively studied populations without identifiable risk factors for liver disease **range from 29-35 IU/L for males** and **19-25 IU/L for females**
  - Normal ALT level may not exclude significant liver disease
- There is a linear relationship between ALT level and BMI that should be assessed
- AST and ALT ULN ranges can vary between different labs
- Elevated ALT or AST above the ULN in a population without identifiable risk factors is associated with increased liver-related mortality

1. Terrault. Hepatology. 2018;67:1560. 2. EASL. J Hepatol. 2017;67:370.

Slide credit: clinicaloptions.com

AASLD Guidance: HBeAg-Positive Chronic HBV Infection

Noncirrhotic HBeAg-Positive Patients With CHB

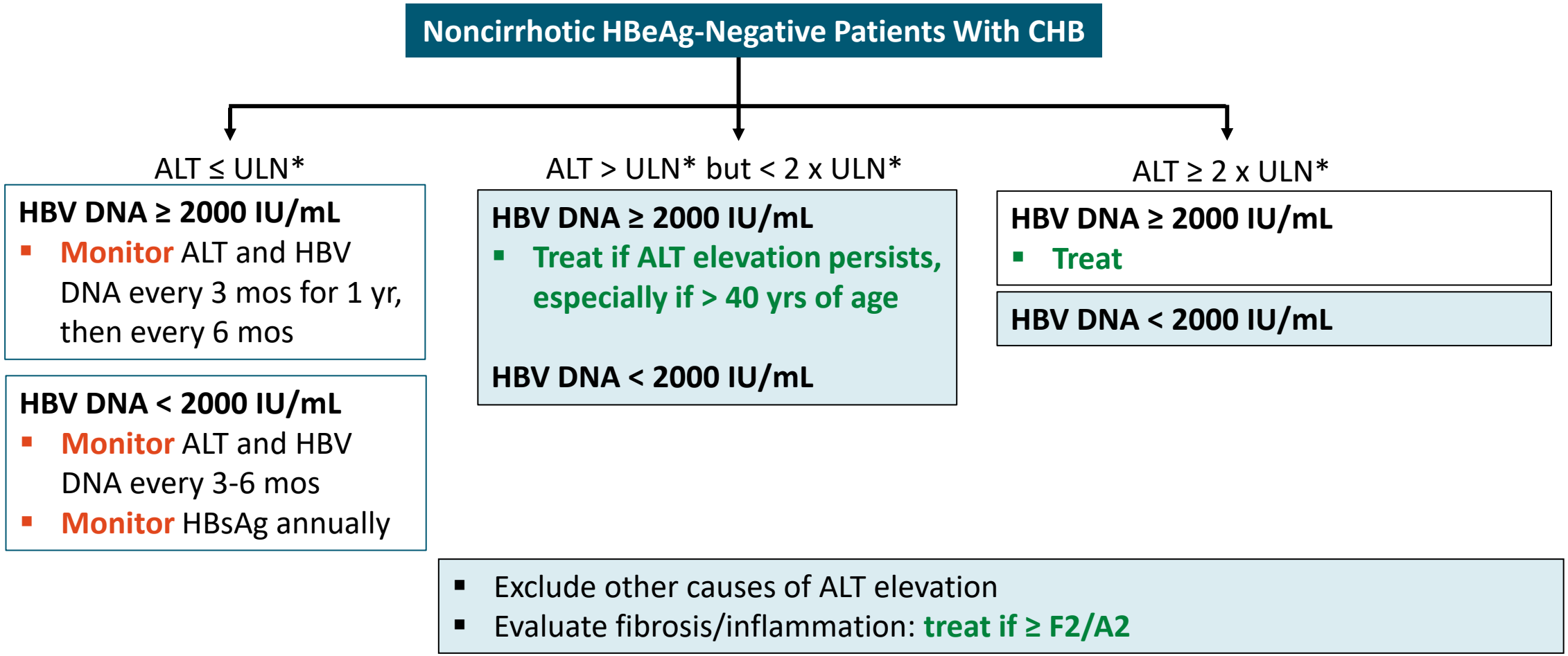
ALT ≤ ULN*	ALT > ULN* but < 2 x ULN*	ALT ≥ 2 x ULN*
HBV DNA > 20,000 IU/mL ▪ **Monitor** ALT and HBV DNA every 3-6 mos, HBeAg every 6-12 mos	**HBV DNA > 20,000 IU/mL** **Note: HBV DNA 2000-20,000 IU/mL may represent seroconversion** ▪ **Monitor** HBV DNA every 1-3 mos and **treat if HBV DNA > 2000 IU/mL persists for > 6 mos**	**HBV DNA > 20,000 IU/mL** ▪ **Treat** **HBV DNA 2000-20,000 IU/mL may represent seroconversion** ▪ **Monitor** HBV DNA every 1-3 mos and **treat if HBV DNA > 2000 IU/mL persists for > 6 mos**

- Exclude other causes of ALT elevation: **treat if ALT elevation persists, especially if > 40 yrs of age**
- Evaluate fibrosis/inflammation: **treat if ≥ F2/A2**

*ALT ULN of 35 IU/L for males and 25 IU/L for females recommended.

Terrault. Hepatology. 2018;67:1560.

AASLD Guidance: HBeAg-Negative Chronic HBV Infection



*ALT ULN of 35 IU/L for males and 25 IU/L for females recommended.

Terrault. Hepatology. 2018;67:1560.

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AASLD Guidance: Patients With Cirrhosis

- Persons with **compensated cirrhosis** and HBV DNA level > 2000 IU/mL are treated per recommendations for immune active CHB → treatment recommended
- Patients with low-level viremia (HBV DNA < 2000 IU/mL) and **compensated cirrhosis** should be treated, regardless of ALT
- All patients with **decompensated cirrhosis** who are HBsAg positive should be treated, regardless of HBV DNA, HBeAg status, or ALT

Terrault. Hepatology. 2018;67:1560.

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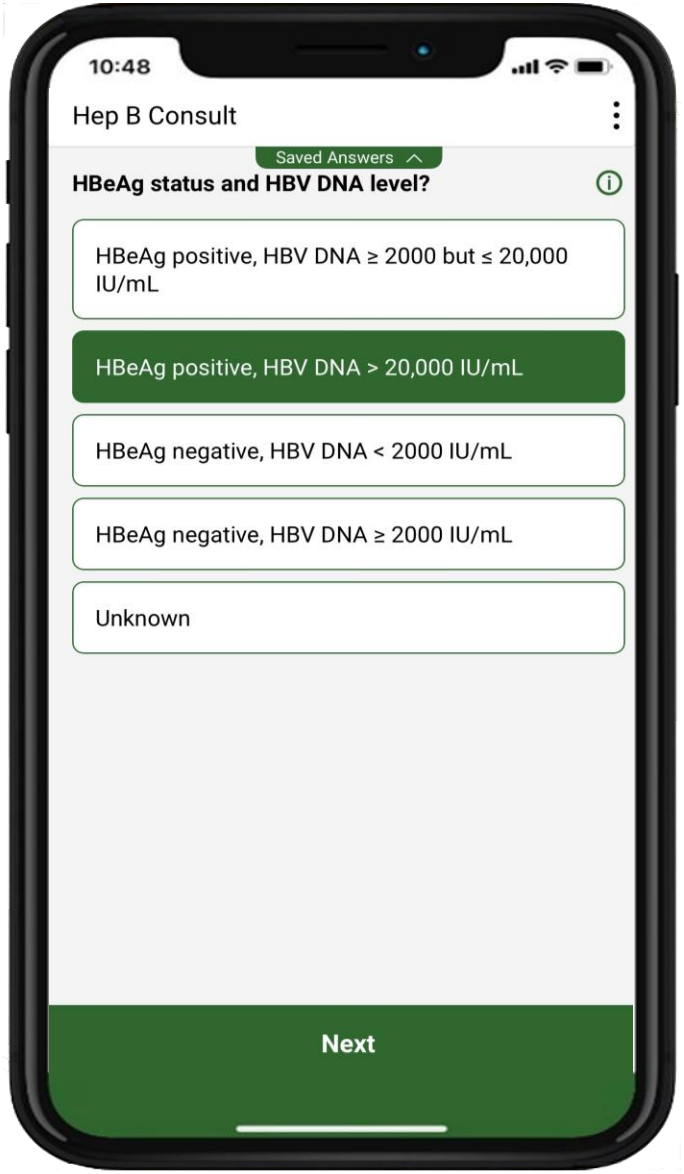

- Case: 35-yr-old man with HBeAg-positive chronic HBV
  - HBV DNA 36,000 IU/mL
  - ALT > ULN but < 2 x ULN
  - Extent of liver fibrosis and inflammation is unknown

Enter your patient characteristics for instant guidance!

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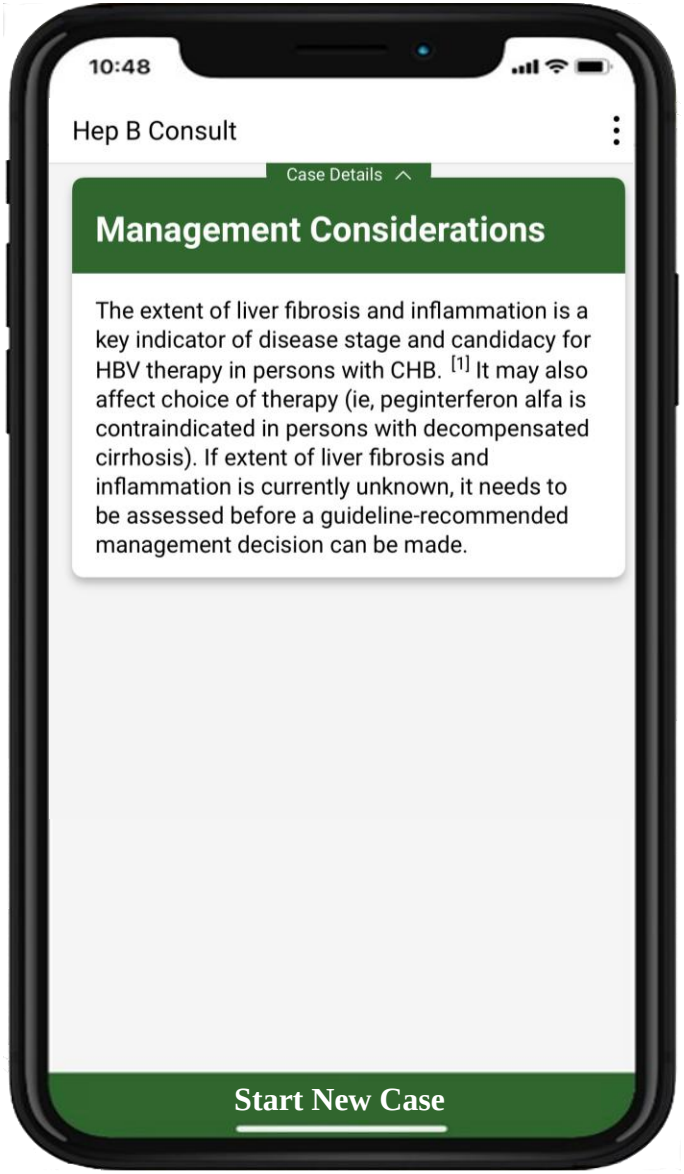

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Selected Noninvasive Tests to Assess for Stage of Liver Fibrosis

Test	Components	Fibrosis Stages Assessed	Requirements	Cost
APRI	AST, platelets	≥ F2, F4 (cirrhosis)	Basic hematology and clinical chemistry	+
FIB-4	Age, AST, ALT, platelets	≥ F3	Basic hematology and clinical chemistry	+
FibroTest	Gamma glutamyl transpeptidase, haptoglobin, bilirubin, A1 apolipoprotein, alpha-2 macroglobulin	≥ F2, ≥ F3, F4 (cirrhosis)	Specialized tests; requires testing at designated laboratories; commercial assay	+ +
FibroScan	Transient elastography	≥ F2, ≥ F3, F4 (cirrhosis)	Dedicated equipment	+ + +

Lurie. World J Gastroenterol. 2015;21:11567.

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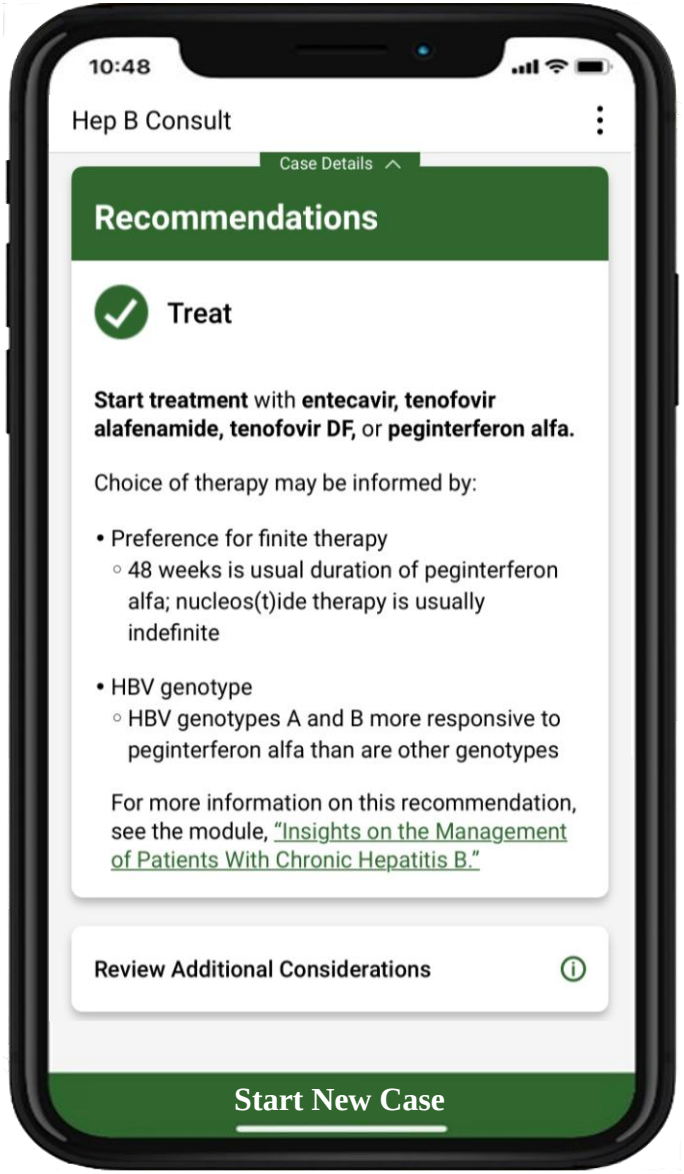

- Case: 35-yr-old man with HBeAg-positive chronic HBV
  - HBV DNA 36,000 IU/mL
  - ALT > ULN but < 2 x ULN
  - ***FibroScan* indicates moderate fibrosis**

Enter your patient characteristics for instant guidance!

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First-line Treatment Options for CHB

Status	Treatment	Notes
Preferred	ETV, TAF*, or TDF†	▪ High potency, high genetic barrier to resistance
	PegIFN	▪ Less safe with cirrhosis (reserve for mild CHB), contraindicated with decompensated cirrhosis
Not preferred	LAM, ADV, or TBV	▪ Low genetic barrier to resistance

*Efficacy and safety of TAF have not been established for CHB in patients with decompensated cirrhosis, pregnant women, or children; recommendations for these populations are subsequently limited. †If TDF is chosen, monitor renal function and BMD in at-risk patients.

ETV, TAF, and TDF have very favorable safety and resistance profiles

Terrault. Hepatology. 2018;67:1560. EASL. J Hepatol. 2017;67:370.

Key Take-home Points

- Assessing treatment candidacy for hepatitis B should include:
  - ALT levels, HBeAg status, HBV DNA level, fibrosis assessment, and family history
- Patients with elevated HBV DNA (>20,000 IU/mL for HBeAg+ and > 2000 IU/mL for HBeAg-) plus elevated ALT and/or significant disease on elastography or liver biopsy should be considered
  - ALT ULN for range from 29-35 IU/L for males and 19-25 IU/L for females
  - Incorporate fibrosis assessment into evaluation of patients with hepatitis B
- Consider family history and comorbidities

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