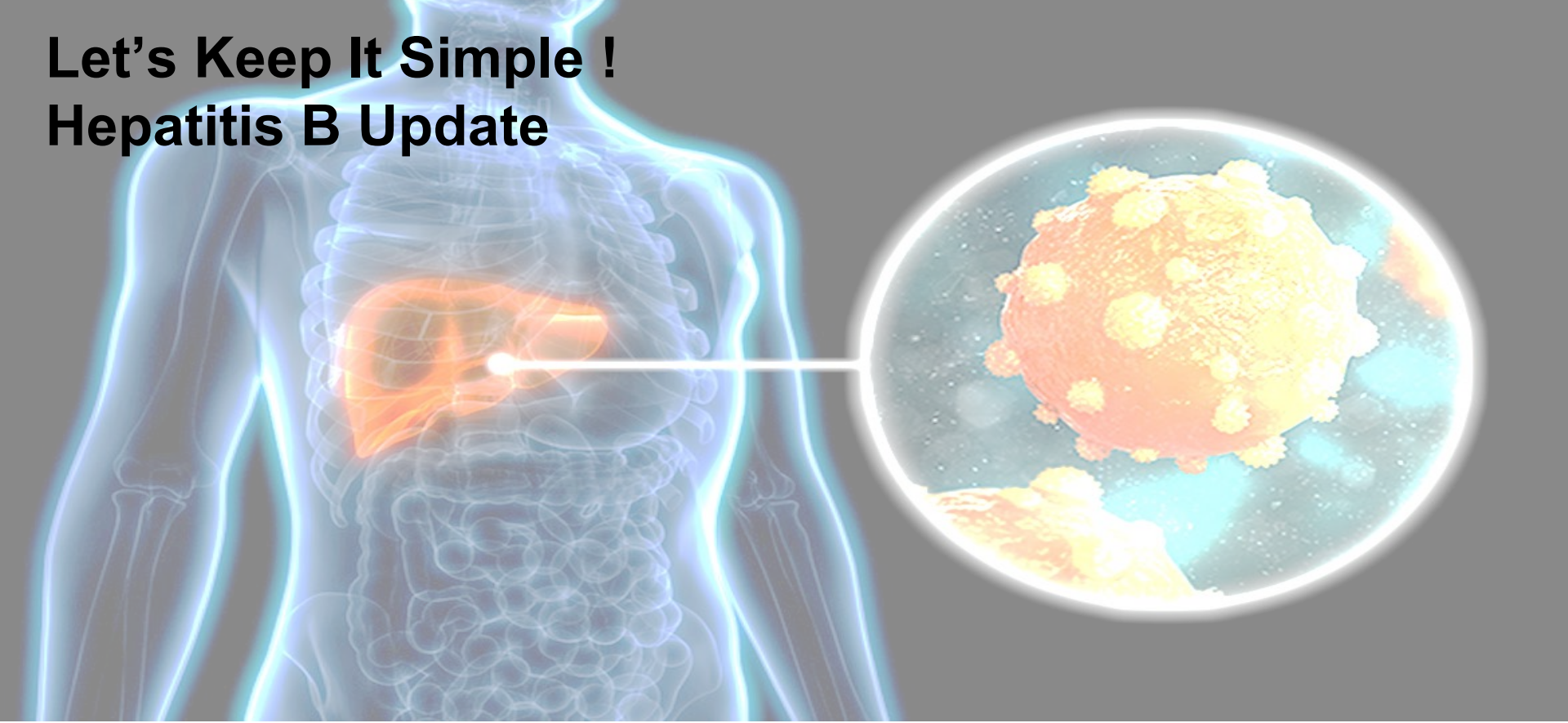
Let’s Keep It Simple !
Hepatitis B Update



Asma Siddique

11/8/2025

Virginia Mason Franciscan Health™
A member of CommonSpirit

Objectives

Understanding the epidemiology and natural history of Hepatitis B

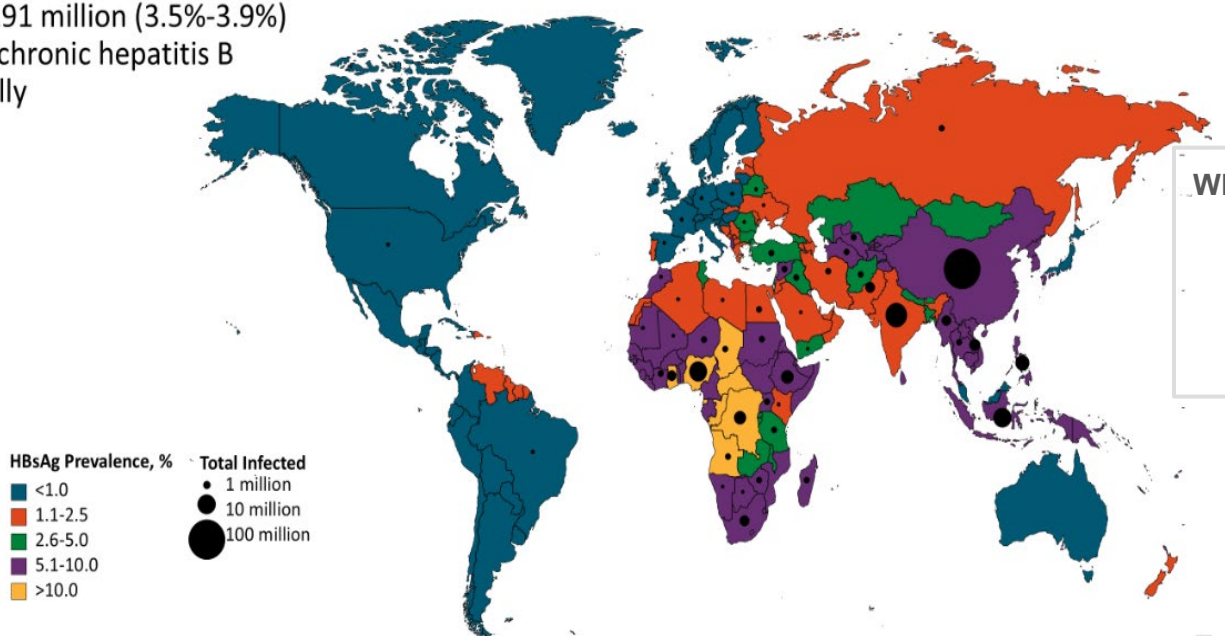
Interpret the various laboratory tests used to diagnose Hepatitis B

Review Hepatitis B vaccination and screening

Discuss novel Hepatitis B investigational therapies

Epidemiology

- 257-291 million (3.5%-3.9%) have chronic hepatitis B globally



WHO estimates

- 254 million living with ch HBV in 2022
- 1.2 million new infections each year
- 1.1 million deaths in 2022
- Highest burden sub-saharan africa, East Asia, Pacific Islands

Only 13% diagnosed and 3% on treatment

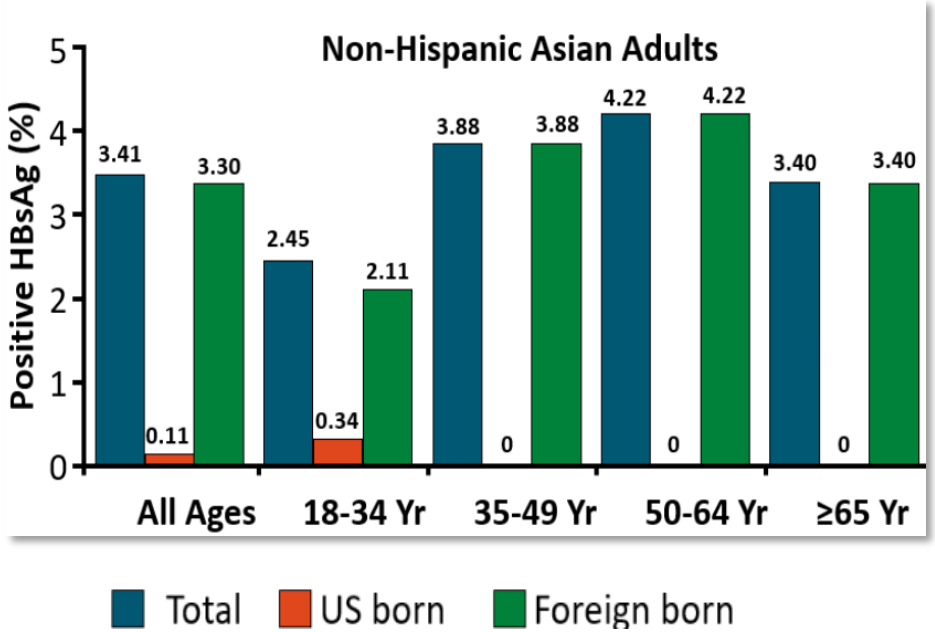
Virginia Mason Franciscan Health
A member of CommonSpirit

WHO. Global Hepatitis Report 2017. who.int/publications/i/item/global-hepatitis-report-2017
Polaris Observatory Collaborators. Lancet Gastroenterol & Hepatol. 2018;3:383.

Slide credit: clinicaloptions.com

CHRONIC HEPATITIS B – Prevalence in US

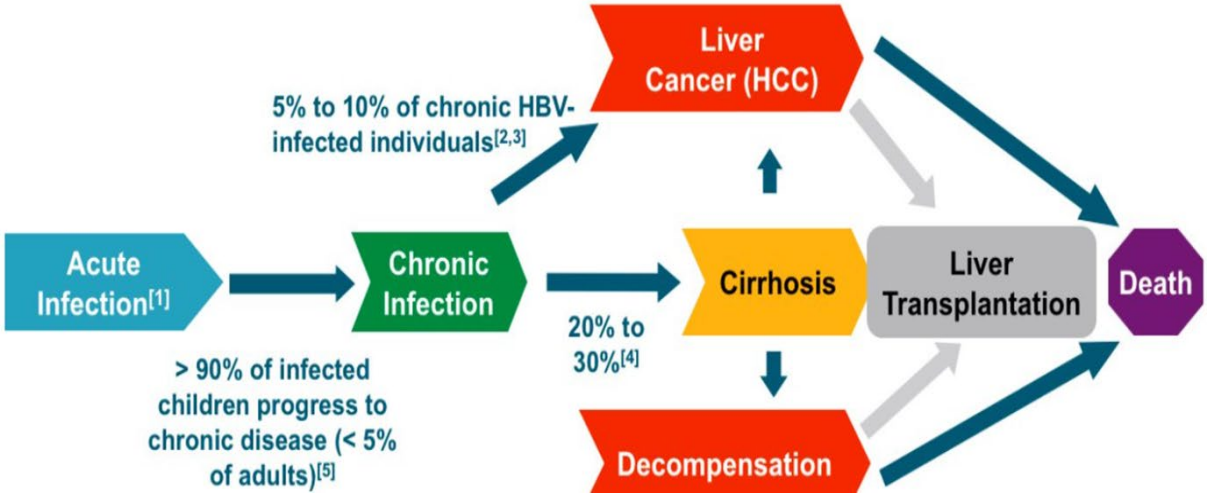
Highest in both foreign-born and US-born Asian adults , followed by Black adults



Virginia Mason Franciscan Health
A member of CommonSpirit

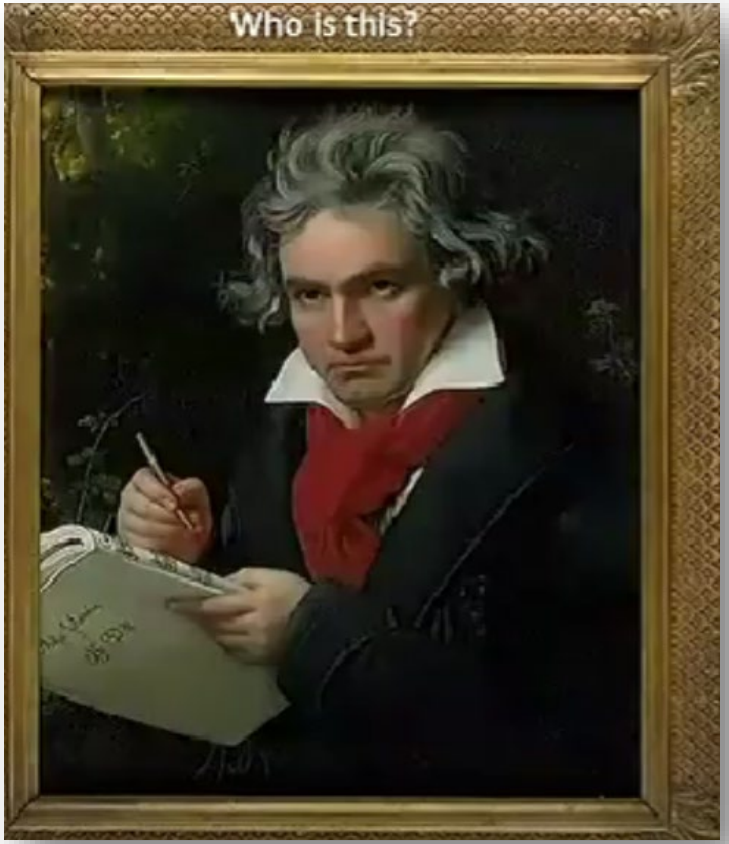
Le.Hepatology. 2020:71:431

Hepatitis B Disease Progression



Virginia Mason Franciscan Health™
A member of CommonSpirit

1.Buckley. Eliminating the public health problem of hepatitis B and C in the United States: Phase One Report. 2016
2.Iloeje. Liver Int. 2012;32:1333
3.Fattovich. Hepatology. 1995;21:77
4.Niederau. World J Gastroenterol. 2014;20:11595
5.Weinbaum. MMWR Recomm Rep. 2008:57:1



Ludwig Van Beethoven (1770-1827)

One of the earliest famous person with confirmed HBV infection

In 2023 - study of Beethovens hair revealed hepatitis B virus DNA , confirming he had HBV

Also h/o heavy alcohol use

Also had 2 genes that cause liver disease - PNP-LA3, HFE

Baruch Samuel Blumberg (1925-2011)

Blumberg's Discovery of Hepatitis B

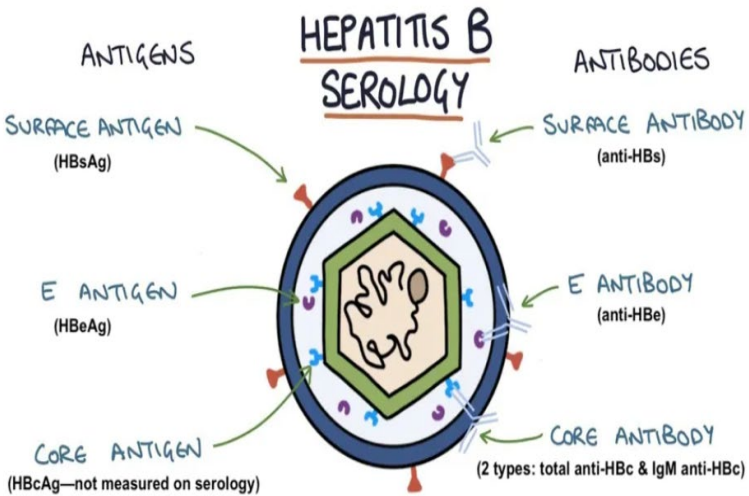
Studying blood from American hemophiliacs - Australian antigen (first patient Australian Aborigine patient)

In 1967, Blumberg noticed the Australia antigen kept appearing in patients with Down syndrome living in institutional care facilities. These patients had high exposure to shared needles and close living conditions

> This clue shifted the thinking: The antigen wasn't a genetic variant — it was a marker of an infectious disease.

His Birthday July 28th → World Hepatitis B Day

Hepatitis B serology



Marker	What is it	Interpretation
HBsAg	Protein on the surface of HBV	Indicates individual is infected
HBsAb	Antibody produced by the body in response to HBsAg	Indicates recovery and immunity, only marker of successful vaccination
HBcAg	Found in the nucleus and therefore not directly detectable	
HBcAb	Produced against HBcAg	Marker of prior exposure cIgM -recent infection
HBeAg	Found between the core and viral membrane	Marker of viral replication and infectivity
HBeAb	Antibody to HBeAg	Predicts emergence of precore or core promoter mutant and transition to chronic HBeAg negative in those not on treatment or long-term clearance of HBV in those on treatment

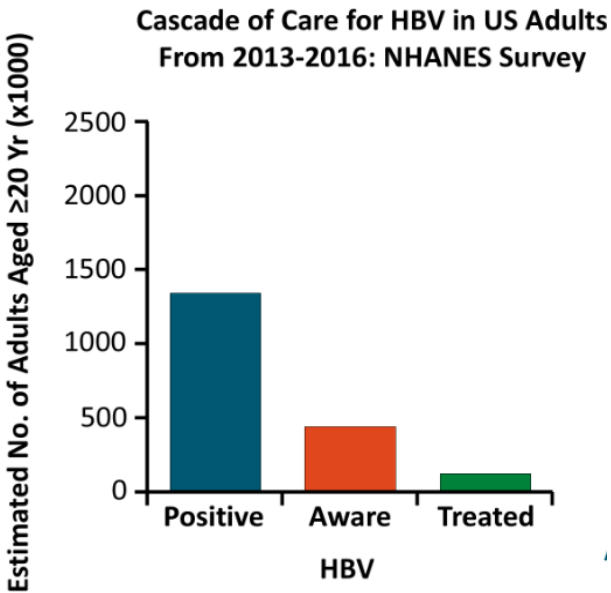
WHO: Global Call For HBV Elimination

Goal to eliminate viral hepatitis as a major global public health threat by 2030; HBV targets include:

-eliminate mother to child transmission
-expand the population we treat
-link patient to care

Virginia Mason Franciscan Health
A member of CommonSpirit

Gaps In HBV Treatment in the US



Addressing The Gaps

PREVENTION — New Vaccination guidelines- vaccinate all adults 18-59yrs

SCREENING — Universal Screening -ALL adults at least once

TREATMENT — Simplified treatment algorithms

Virginia Mason Franciscan Health
A member of CommonSpirit

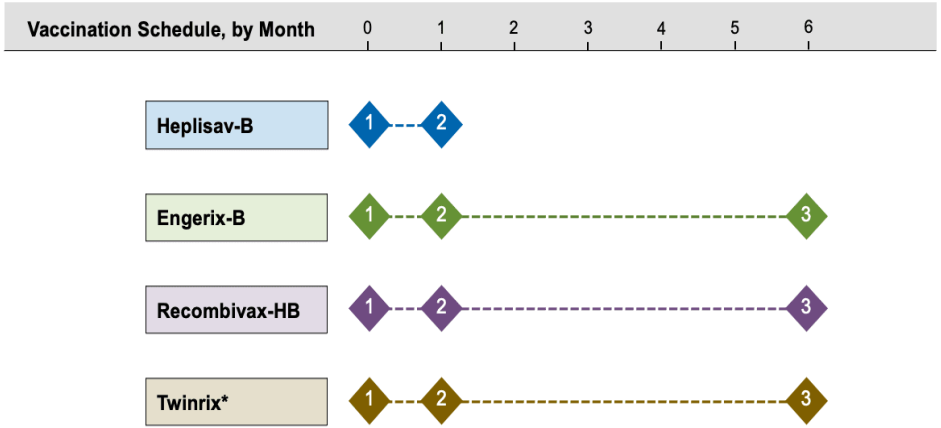
Zhou. Clin Gatroenterol Hepatol. 2020;18:188. Khalili. JAMA Netw Open. 2023;6:e237018.

HBV - Who Should Be Vaccinated

- All infants.
- Unvaccinated children younger than 19 years of age.
- Adults 19–59 years.
- Adults 60 years and older with risk factors for hepatitis B.
- The following groups may also receive HepB vaccination:
  - Adults 60 years and older without known risk factors for hepatitis B.

Virginia Mason Franciscan Health
A member of CommonSpirit

Choice and Schedule Of Hepatitis B Vaccine in Adults



Heplisav: 2 doses , 1 month apart
90-95% seroprotection

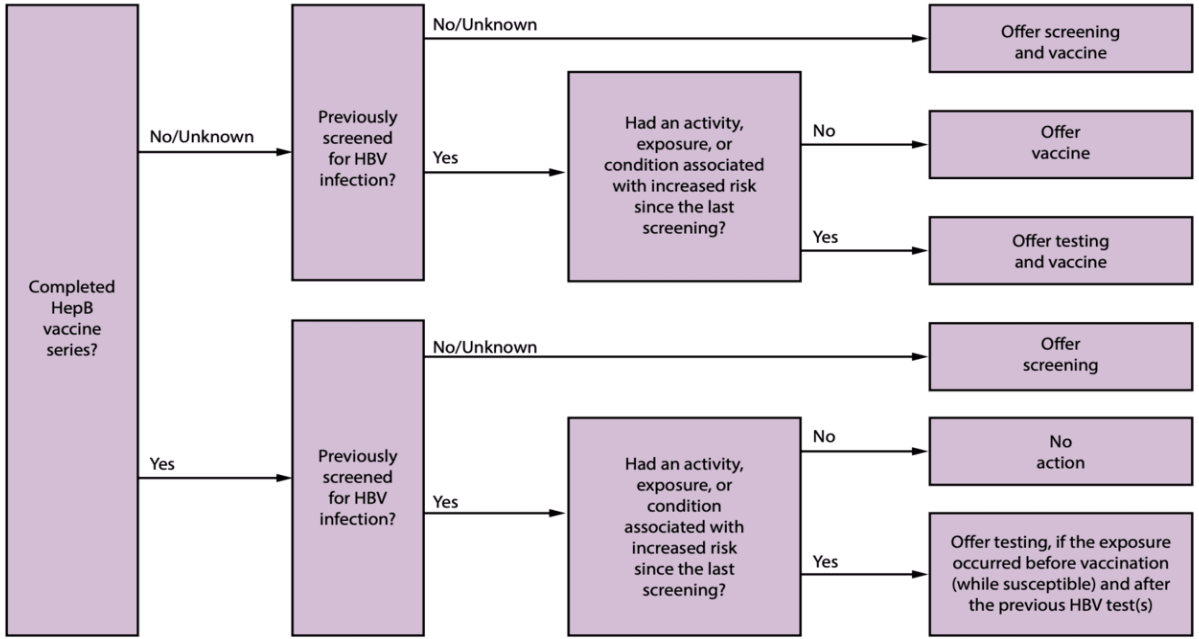
Twinrix for HAV + HBV

***Before a potential exposure, such as travel, Twinrix can be administered as an accelerated series at days 1, 7, 21-30, followed by a fourth dose at 12 months.**

Virginia Mason Franciscan Health
A member of CommonSpirit

Modfied from: Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31.

Incorporating HBV Screening In Clinical Workflow (nonpregnant Adults)



Virginia Mason Franciscan Health
A member of CommonSpirit

HBV Screening

Universal Hepatitis B Screening – all adults 18 -59 years of age once in a lifetime

If HBV Positive —> Universal HDV Screening

Virginia Mason Franciscan Health
A member of CommonSpirit

HBV Serology: Initial Testing

- **Hepatitis B surface antigen (HBsAg)**

  Present in active infection; Chronic infection positive > 6 months

  Quantitative tests are available

  – Predictive for successful cessation of nucleosides

  – Predictive for response to novel agents

- **Hepatitis B core total antibody (HBcAB)**

  Indicates prior infection

  There is also core IgM Ab test

- **Hepatitis B surface antibody**

  Marker of immunity; infection or vaccine response

HBV serology: Follow up testing

These are done if HBsAg positive

- Hepatitis B e Antigen

  Surrogate for viral replication

  Traditionally incorporated in treatment algorithm

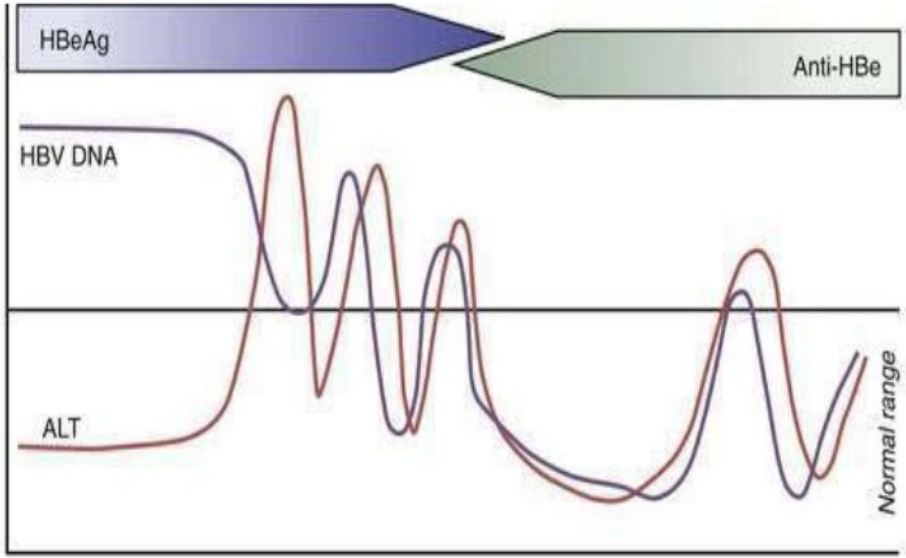
- Hepatitis B e Antibody

- HBV DNA

  Defines active viral replication

  Important component of treatment criteria

Phases Of Chronic Hepatitis B – Old vs New Nomenclature



eAg + chronic infection (immune tolerant CHB)
- Normal serum transaminases
- Normal biopsy
- +sAg, +eAg, ↑↑↑↑ HBV DNA

eAg + chronic hepatitis B (immune active CHB)
- Elevated serum transaminase
- Inflammation and fibrosis on biopsy
- +sAg, +eAg or -eAg, ↑↑ HBV DNA

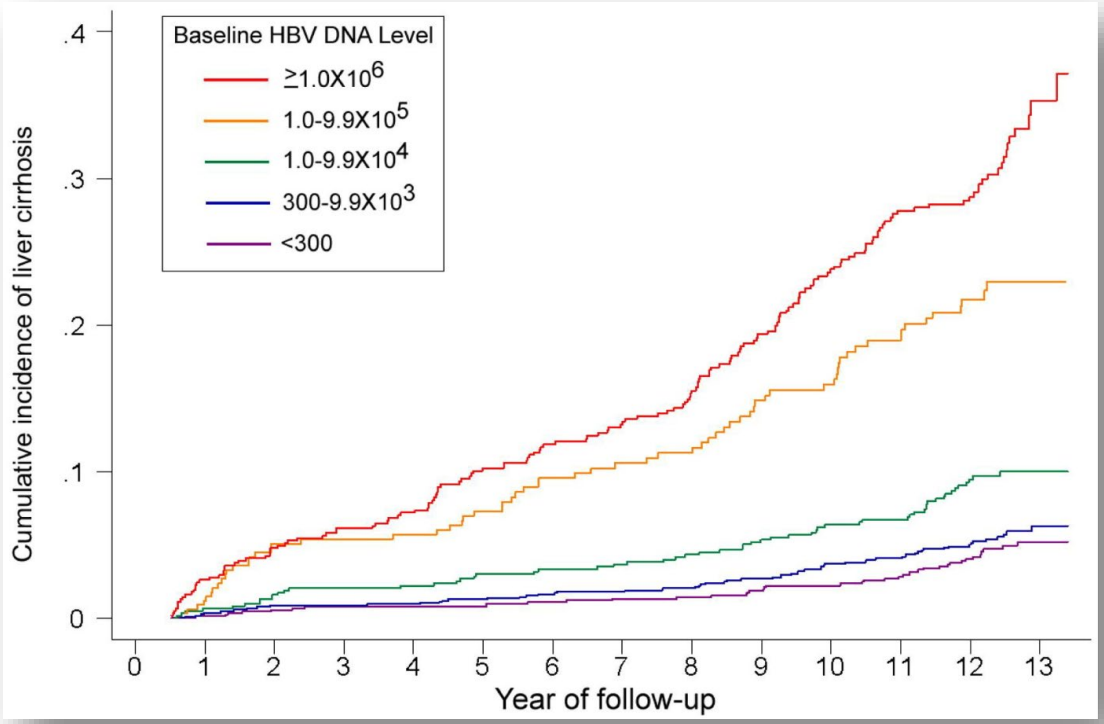
eAg negative chronic infection /hepatitis (inactive carrier and eAg negative hepatitis)
- Variable transaminase elevation
- +sAg, -eAg, +eAb, low HBV DNA

OLD	**Immune Tolerant**	**Immune Clearance**	**Inactive Carrier State**	**Reactivation**
NEW	**HBeAg+ Chronic Infection**	**HBeAg+ Chronic Hepatitis**	**HBeAg- Chronic infection**	**HBeAg- Chronic Hepatitis**

Resolved
-sAg
+sAb

Lok A. Hepatol 2017. EASL HBV Guidelines 2017

HBV DNA and Progression to cirrhosis



Predicting Cirrhosis Risk Based on the Level of Circulating Hepatitis B Viral Load
Iloeje, Uchenna H. et al.
Gastroenterology, Volume 130, Issue 3, 678 - 686

Chronic Hepatitis B - Treatment

Case Study

Julia 31 yr old women from Vietnam . History of rheumatoid arthritis, not on any medications. Seen in hepatology clinic to establish care . States she was diagnosed as a child and both parents, older brother have HBV, no f/h HCC

Asymptomatic , exam -normal

ALT 26, AST 12, AP 129, TB 0.8

HBsAg+, HBeAg + , HBV PCR 160,000 IU/ml

FIbroscan - Stage 0 fibrosis

HBV – TREATMENT GOALS

Reduce morbidity (cirrhosis, hepatic decomp, liver failure, HCC) and improve survival

- persistent suppression of HBV DNA
- HBsAg loss is the ultimate goal of therapy.
- Normalisation of ALT is an additional endpoint.

Additional goals of antiviral therapy

- improvement of liver fibrosis
- improvement of health-related quality of life and patient-reported outcomes
- prevention of HBV transmission
- prevention of HBV reactivation and/or hepatitis

TREATMENT GUIDELINES

Treat Active CHB (+/-HBeAG) if…..

- ❑ Advanced Fibrosis/Cirrhosis
- ❑ Co-infection HIV /HDV
- ❑ Extrahepatic manifestations
- ❑ F/H of HCC
- ❑ Special popln: patients on immunosuppressant, pregnancy

Criteria	AASLD[1] 2018	APASL[2] 2016		EASL[3] 2017
HBeAg Positive				
HBV DNA, IU/mL	>20,000	>20,000	>20,000	>2000
ALT	≥2x ULN	>2x ULN	>2x ULN	> ULN
Liver biopsy				≥ moderate necroinflammation ± fibrosis
HBeAg Negative				
HBV DNA, IU/mL	>2000	>2000	>20,000	>2000
ALT	≥2x ULN	>2x ULN	>2x ULN	> ULN
Liver biopsy				≥ moderate necroinflammation ± fibrosis

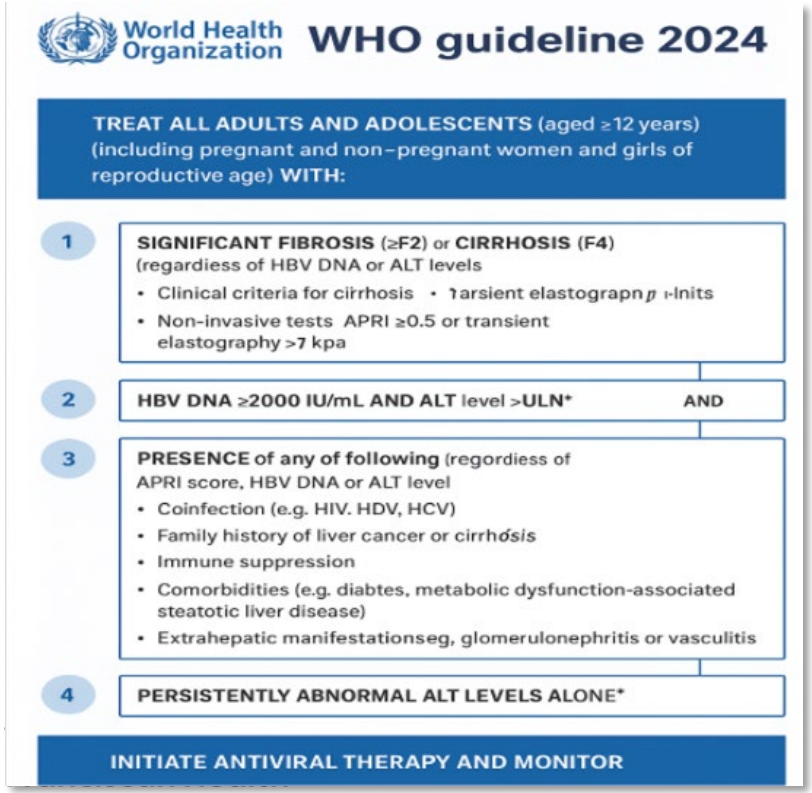
- **Normal ALT (AASLD):** ≤35 U/L (men); ≤25 U/L (women)
- **Normal ALT (APASL and EASL):** <40 U/L

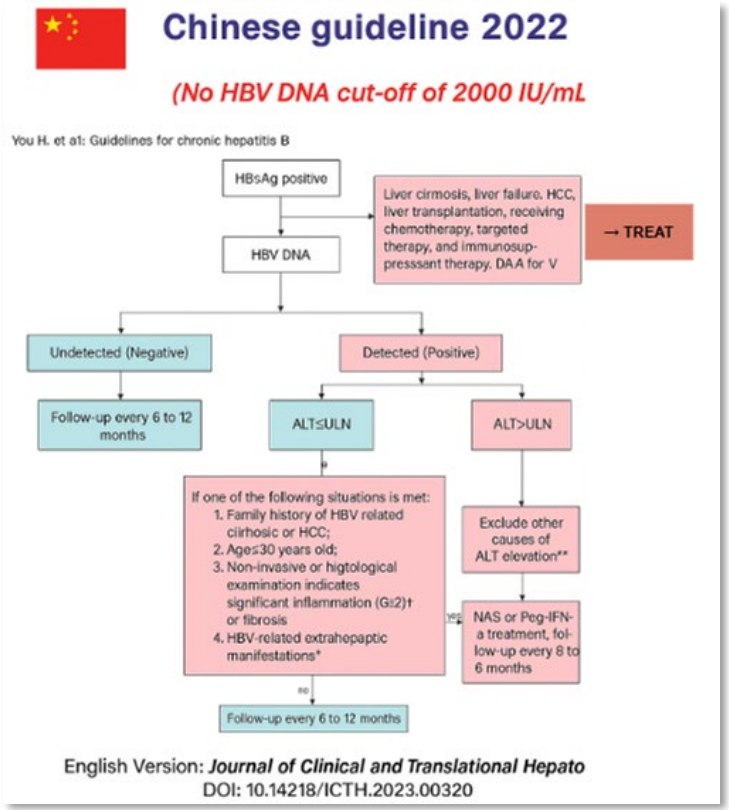
Virginia Mason Franciscan Health
A member of CommonSpirit

1. Terrault. Hepatology. 2018;67:1560. 2. Sarin. Hepatol Int. 2016;10:1. 3. EASL. J Hepatol. 2017;67:370.

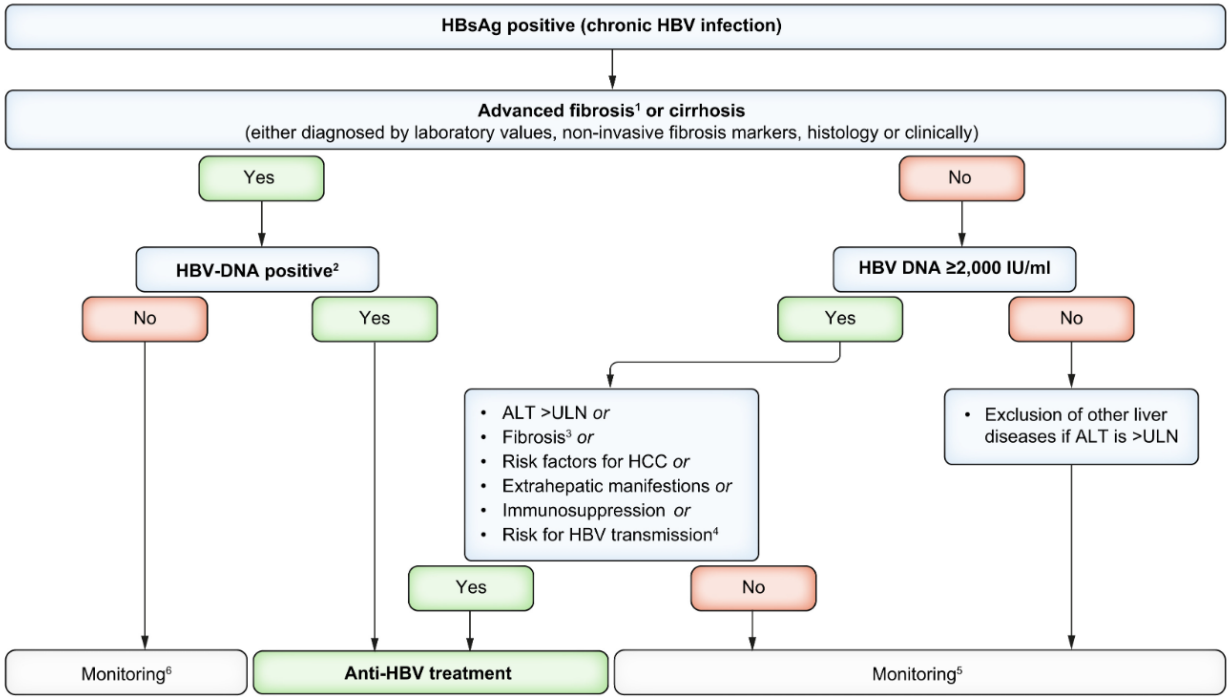
Slide credit: clinicaloptions.com

INTERNATIONAL RECOMMENDATIONS





EASL TREATMENT GUIDELINES



All HBsAg positive individuals with detectable HBV DNA are candidates for antiviral therapy

th HBV DNA ≥200,000 IU/ml

6. Anti-HBV treatment in immunosuppression

Simplified Treatment Algorithm

TREAT

Age, Yr	HBV DNA, IU/mL	ALT, U/L
≥30	>2000	Any ALT level
<30	>2000	> ULN (females: > 19U/L, males: >30 U/L)

DEFER

Age, Yr	HBV DNA, IU/ml	ALT, U/L
–	< 2000	-
< 30	> 2000	< ULN

Treat all patients with cirrhosis and detectable viral load

Virginia Mason Franciscan Health
A member of CommonSpirit

Dieterich. Gastro Hep Adv. 2023;2:209.

Re-defining Treatment Goal

Current Goal

- Viral suppression
- Decrease risk of progression to cirrhosis
- Decrease risk of HCC

Functional Cure

- Sustained HBsAg loss
- Undetectable HBV DNA
- +/- HBsAb

Complete Cure

- Erradicating all traces of HBV from the liver (inc cccDNA, integrated HBV DNA

Two therapeutic options for treatment of chronic HBV infection: NAs or PEG-IFNα

Features	ETV,tenofovir (TDF, TAF)	PEG-IFN α
Strategy	Preventing disease progression by suppressing HBV	Induction of long term immune control
Administration	Oral, once daily	Subcutaneous, once weekly
Treatment duration	Long-term	Finite (48 weeks)
Response to treatment	eAg loss low to moderate sAg loss low	eAg loss moderate sAg low, better than NA
Side effects	Very Low	Moderate to high
Contraindications	Very few (eg ETV in pregnancy)	Numerous

Virginia Mason Franciscan Health
A member of CommonSpirit

EASL Clinical Practice Guidelines on the management of hepatitis B virus infection Cornberg, Markus et al.
Journal of Hepatology, Volume 83, Issue 2, 502 - 583

First-Line HBV Treatment

Oral NA's – Highly effective, favourable safety profile, oral, once daily

Entecavir	Access/cost - generic Avoid if h/o lamivudine resistance
Tenofovir alafenamide(TAF)	More expensive Preferred renal dysfunction or bone disease
Tenofovir disoproxil fumarate (TDF)	Access/cost - generic Preferred pregnancy Avoid if CrCl <15ml/min/ dialysis

Not preferred -LAM, ADV, TBV

Virginia Mason Franciscan Health
A member of CommonSpirit

Stopping HBV NA Therapy

Cirrhosis

Indefinite therapy

HBeAg-positive CHB

- Until HBeAg seroconversion, undetectable HBV DNA, ALT normalization plus ≥1 yr consolidation
- Alternative: until HBsAg loss

HBeAg-negative CHB

- Indefinite therapy, unless strong compelling rationale for treatment discontinuation

Virginia Mason Franciscan Health
A member of CommonSpirit

2025 AASLD draft guidelines suggest to not withdraw NA until HBsAg loss

Quantitative HBsAg- marker of amount/activity of cccDNA

Prognostic Value	DNA level < 2000 IU/mL and an HBsAg level < 1000 IU/mL - inactive carrierThese HBV DNA and qHBsAg cutoffs have also been associated with a lower risk for HCC and liver disease progression
HBsAg clearance	Very low HBsAg (< 100 IU/mL) in combination with an HBV DNA < 2000 IU/mL have a high probability of spontaneous HBsAg clearance
Identify inactive HBV carriers	"gray zone"—HBV DNA or ALT levels borderline between inactive infection and immune-active HBeAg-negative CHB—may be differentiated with a 1-time qHBsAg test assessed in combination with their HBV DNA level
Monitor Rx Stopping rule	pegINF -if no drop HBsAg by wk24-ineffecive treatment NA data limited - eAg pt if 1log drop in qHBsAg - higher rate of HBsAg clearance <100 IU/mL may be a useful cutoff for deciding to stop therapy

High HBsAg levels can predict the same outcomes as high HBV DNA levels

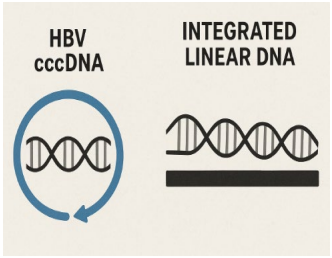
1. Vachon. Viruses. 2021;13:951. 3. Brunetto. Gastroenterology. 2010;139:
3. Chan. J Hepatol. 2011;55:1121. 4. Brouwer. Clin Gastoenterol Hepatol. 2

CHRONIC HEPATITIS B

AND

HEPATOCELLULAR CARCINOMA

Time for some basic science…



Covalently Closed Circular DNA (cccDNA)

- After HBV infects the hepatocyte, **relaxed circular DNA (rcDNA)** from the viral particle is delivered into the nucleus.- **covalently closed circular DNA (cccDNA)**
- cccDNA serves as the template for producing all viral RNA and proteins needed to make new viruses

Why it's a problem: cccDNA cannot be easily eliminated by current antiviral therapies, making it the primary obstacle to a complete cure for chronic HBV infection.

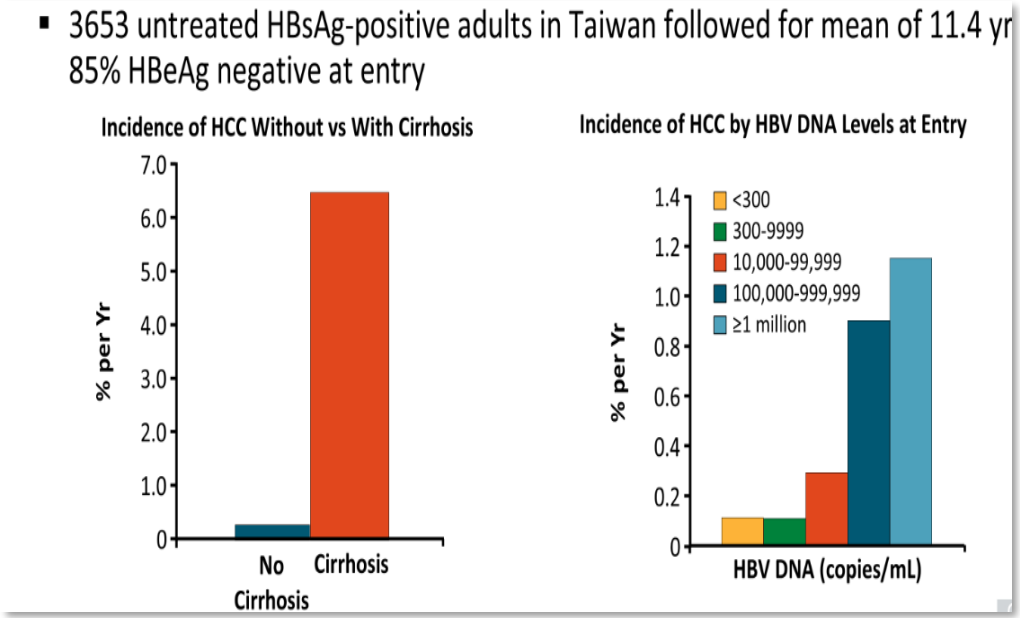
Linear DNA Integration

- Fragments of HBV DNA break and insert itself into the DNA host hepatocyte genome.
- Integrated DNA cannot produce new infectious viral particles, since the full viral genome isn't intact.
  But it can still produce viral proteins (especially HBsAg).
  This contributes to persistent surface antigenemia (HBsAg in blood) even if viral replication is low or suppressed.
- Integrated DNA can also **disrupt host tumor suppressor genes , cause chromosomal instability** → linked to the development of **hepatocellular carcinoma**

cccDNA ensures the persistence of HBV infection by replicating within the nucleus
Integration of viral DNA into host genome can initiate or promote development of HCC

REVEAL: High Viral Load Associated With Increased Incidence of HCC

- 3653 untreated HBsAg-positive adults in Taiwan followed for mean of 11.4 yr
  85% HBeAg negative at entry



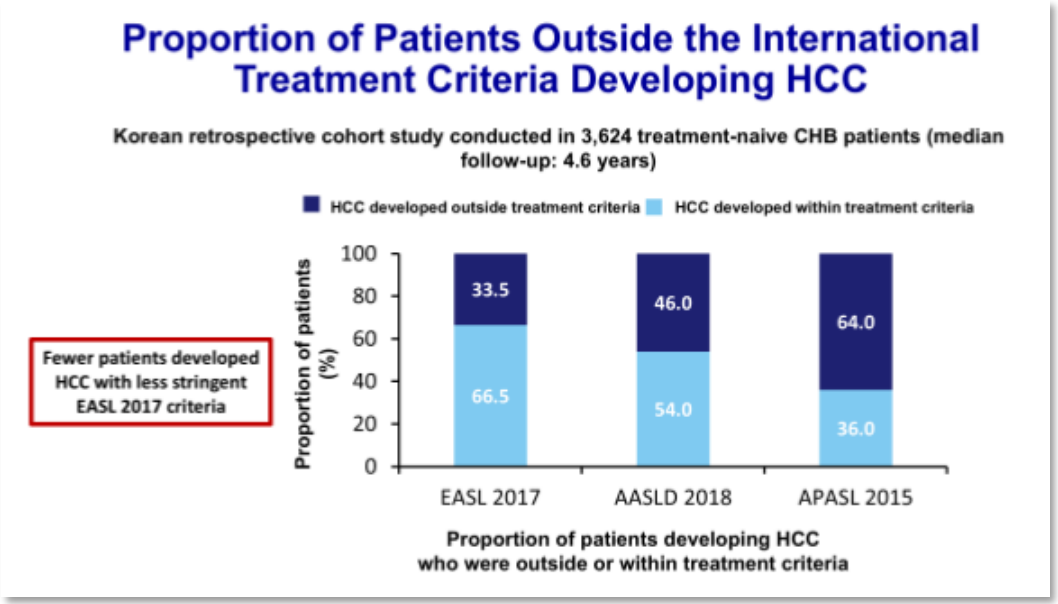
Risk Factors for HCC

- HBV DNA >2000 IU/ml
- qHBsAg > 1000
- eAg +ve and >30yr
- Co-infection (HDV, HIV, HCV)
- Core promoter mutation
- Genotype C
- Cirrhosis
- f/h HCC

Virginia Mason Franciscan Health
A member of CommonSpirit

Chen. JAMA. 2006;295:65.

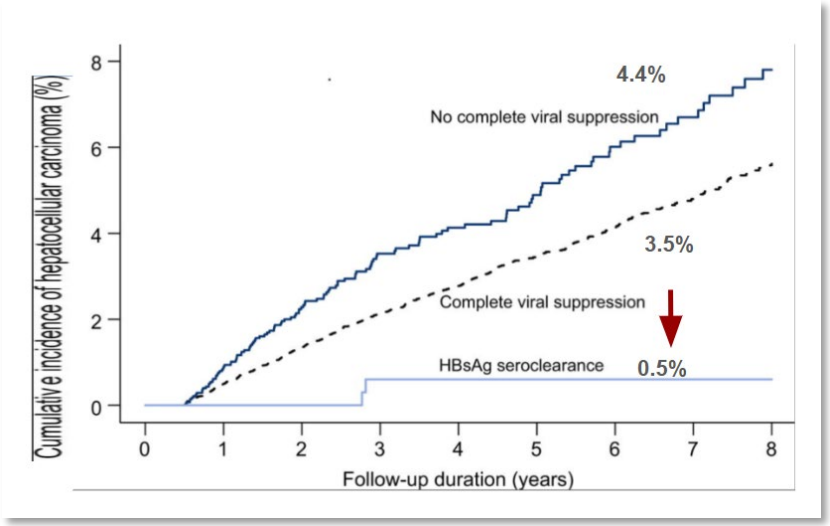
HCC in Patients with Low HBV DNA



Virginia Mason Franciscan Health
A member of CommonSpirit

Sinn et al J Viral Hepat 2019

Liver Cancer Risk: Suppression is good, HBsAg clearance ideal



20,263 NA-treated patients with HBV
Followup: 4.8 years
86.4% - viral suppression
2.1 % - HBsAg clearance

Incidence of HCC lowest in those who achieve HBsAg-loss

Virginia Mason Franciscan Health
A member of CommonSpirit

Yip TCK et al J Hepatology 2019: 70 - 361-370

Hepatocellular Carcinoma Guidance

WHO	HOW	WHEN
Cirrhosis (any etiology) **HBV** • Persons from Africa >20 • Men >40 • Women > 50 • Family h/o HCC • Coinfection HDV	Ultrasound + AFP	Every 6 months

Strong association between viral load and HCC
Quantitative viral load in the driver of HCC
Lower the risk by treating

Virginia Mason Franciscan Health
A member of CommonSpirit

Case Study

Julia 31 yr old women from Vietnam . History of rheumatoid arthritis, not on any medications. Seen in hepatology clinic to establish care . States she was diagnosed as a child and both parents, older brother have HBV, no f/h HCC

Asymptomatic , exam -normal

ALT 26, AST 12, AP 129, TB 0.8

HBsAg+, HBeAg + , HBV PCR 160,000 IU/ml

Returns for followup and on questioning states her brother was recently diagnosed with HCC

What the management recommendations ? Treat or monitor?

One other reason to treat…
Living with Chronic HBV:Impact on quality of life

Chronic symptoms: joint pain, muscle aches, chronic fatigue

Fear, anxiety and stress

Self isolation and external isolation, depression

Harassment and discrimination

Virginia Mason Franciscan Health
A member of CommonSpirit

Mother - to - Child Transmission (MTCT)

Virginia Mason Franciscan Health
A member of CommonSpirit

HBV – Mother - to - Child Transmission (MTCT

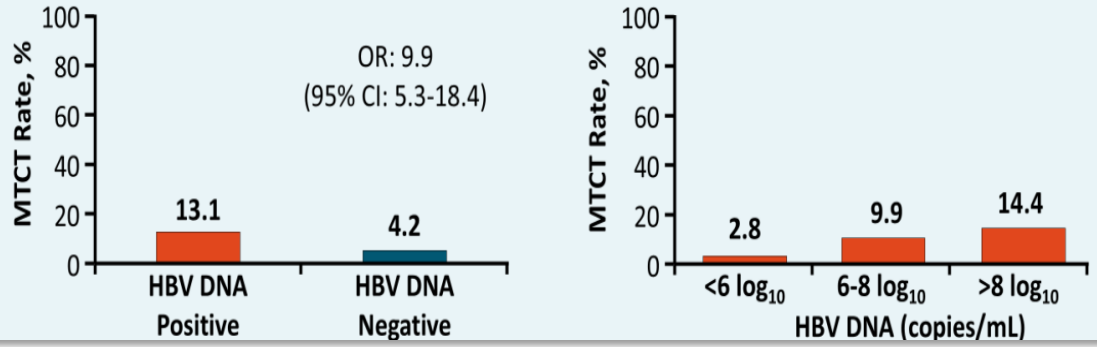
HBsAg positive mother

20% to 40% risk of infant infection by 1 year

HBeAg positive mother

70% to 90% risk of infant infection by 1 year

- MTCT rates are higher in mothers with **positive HBV DNA**, particularly among those with **higher HBV DNA levels**
  - Meta-analysis of HBeAg-positive mothers (N = 10,142 mother-child pairs)



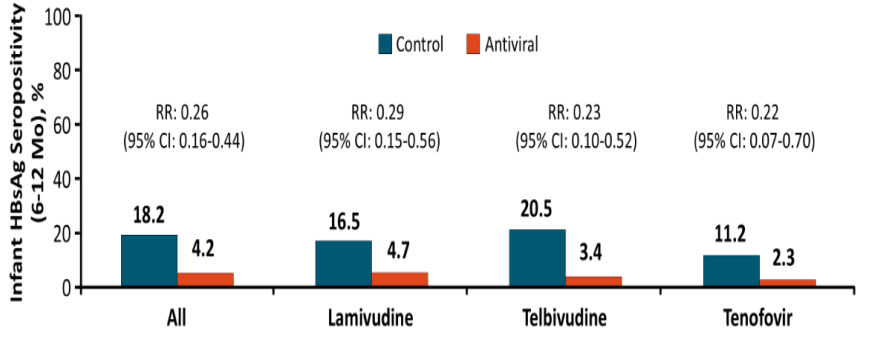
Virginia Mason Franciscan Health
A member of CommonSpirit

Beasley. Am J Epidemiol. 1977;105:94. Chen. Hepatol Res. 2018;48:788.
Kumar. Hepatol Int. 2022;16:211. WHO HBV Guidelines. March 2024.

Slide credit: clinicaloptions.com

Treat To Prevent MTCT

- Meta-analysis of 26 controlled studies in pregnant women with chronic HBV infection treated with antiviral therapy (N = 3622)
  - All antiviral therapies reduced infant HBsAg seropositivity at 6-12 mo
  - No increased adverse maternal or fetal outcome observed



Brown. Hepatology. 2016;63:319-333.

Slide credit: clinicaloptions.com

Preferred Drug- TDF, high potency, no resistance

Virginia Mason Franciscan Health
A member of CommonSpirit

Recommendation for monitoring HBsAg-positive mothers

All pregnant women should be screened for HBV every pregnancy

In HBsAg+ pregnant women

-1st trimester - check LFT, CBC, HBeAg, HBeAb, HBV DNA

-2nd trimester (wk 24-28) - Check ALT, HBV DNA

If HBV DNA < 200,000 IU/ml - monitor

If HBV DNA > 200,000 IU/ml - Start tenofovir

- **HBeAg-positive status** is a **predictor of MTCT**
  - In areas with limited access to HBV DNA, HBeAg can be used to determine treatment eligibility in pregnant people

Consistent with updated 2024 WHO HBV guidelines: administer antiviral prophylaxis for all HBsAg-positive pregnant women with HBV DNA ≥200,000 IU/mL or **positive HBeAg**

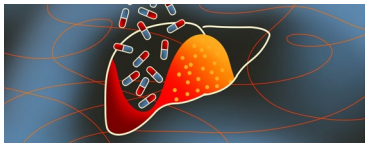
Administer birth dose of HBV vaccination AND HBIG - within 12 hrs of delivery

Immunoprophylaxis - 94% effective !

HBV REACTIVATION - HBVr

Virginia Mason Franciscan Health
A member of CommonSpirit

HBVr - Definition



Abrupt increase or reappearance of HBV DNA ; reverse seroconversion (HBsAG -ve → HBsAg +ve) often triggered by immunosuppressive therapy, chemotherapy, or biologic agents.

Present with rise in liver enzymes (ALT/AST) indicating hepatitis, sometimes leading to severe hepatic injury or liver failure.

Baseline HBV Profile	HBV Reactivation
HBsAg positive HBV DNA low level/undetectable	≥ 1 $\log_{10}$increase in HBV DNA HBV DNA ≥ 1000 IU/ml
HBsAg negative **HBcAb positive** HBV undetectable	HBsAg positive Appearance of HBV DNA

Virginia Mason Franciscan Health
A member of CommonSpirit

Terrault NA. Hepatology 2018

HBVr - Risk Stratification

Establish baseline serology

- **Hepatitis B surface antigen**
- **Hepatitis B core antibody**
- **HBV-DNA**

High Risk → HBVr ≥ 10%

Moderate Risk → HBVr 1 - 10%

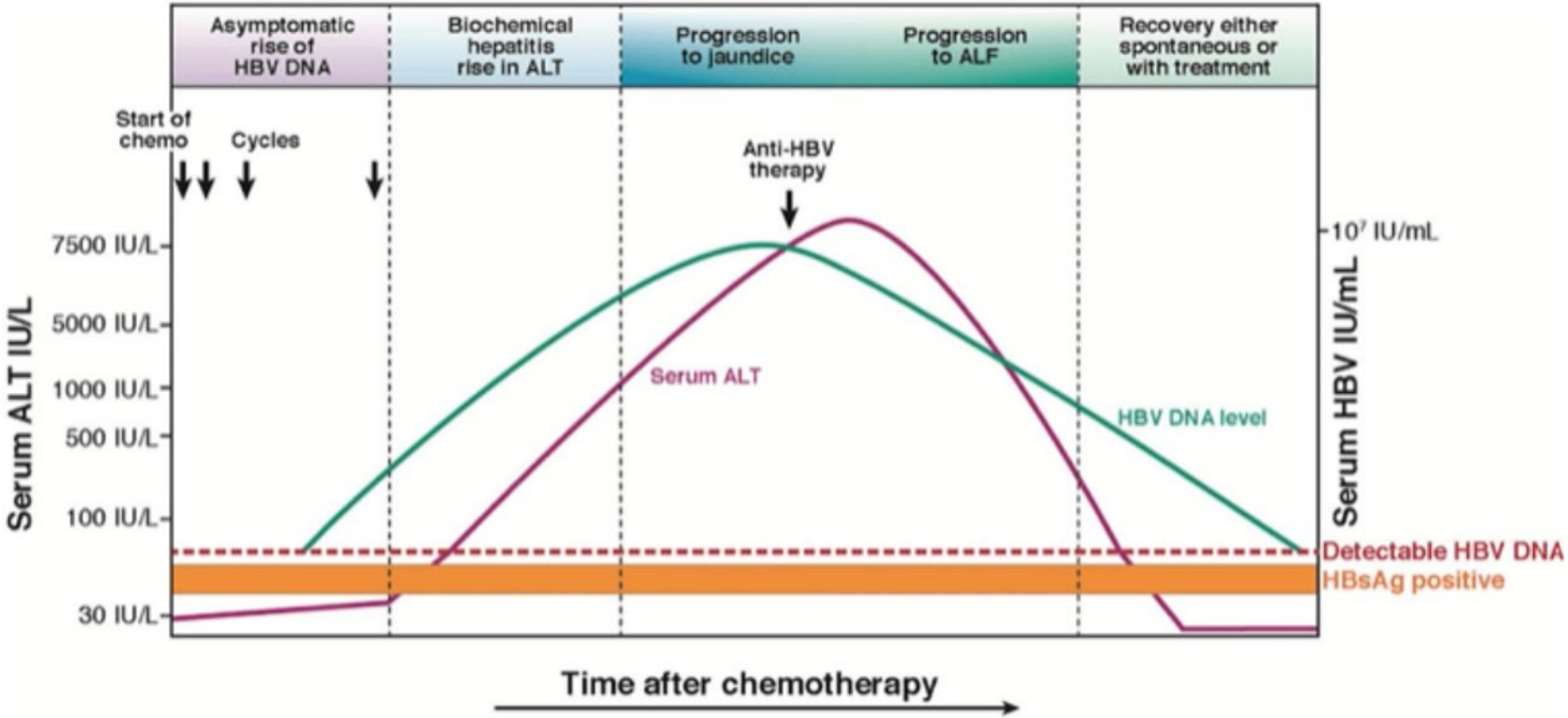
Low Risk → HBVr ≤ 1%

Who is at risk HBVr

- Persons with chronic hepatitis B (HBsAg +, HBcAb +)
- Persons with resolved (HBsAg -, HBcAb +)

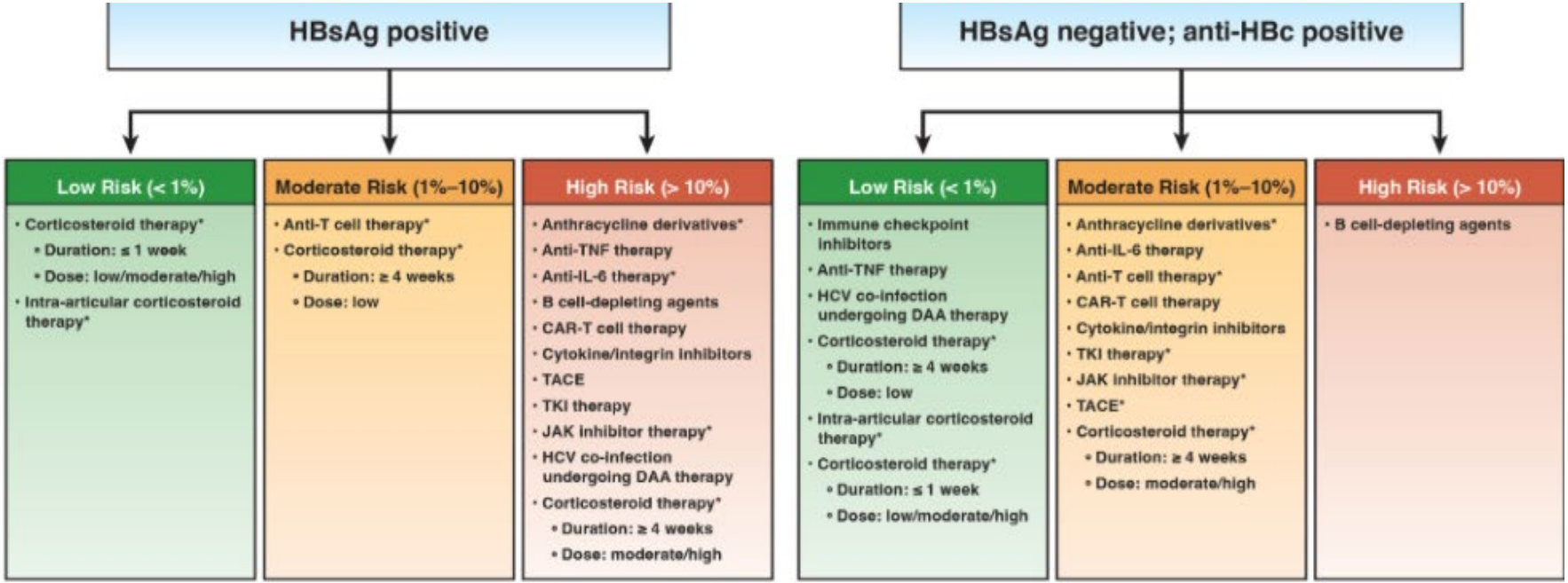
Chemotherapy
Treatment for autoimmune disease
Solid organ or bone marrow transplantation
Direct acting antiviral therapy for HCV
HCC therapy (TACE)
Withdrawal of HBV antiviral therapy

Virginia Mason Franciscan Health
A member of CommonSpirit



Virginia Mason Franciscan Health
A member of CommonSpirit

Loomba et al. Gastroenterol. 2017;152:1297-1309



Rituximab : Highest Risk of HBV Reactivation

Virginia Mason Franciscan Health
A member of CommonSpirit

AGA Clinical Practice Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation in At-Risk Individuals. Ali, Faisal S. et al.. Gastroenterology, Volume 168, Issue 2, 267 - 284

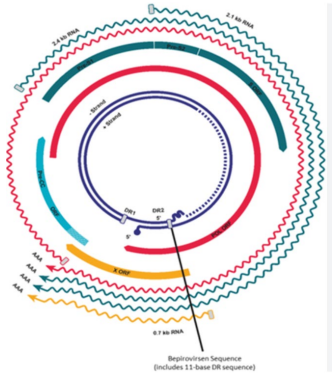
HBV Reactivation : Treat or Monitor

High Risk	**Recommend antiviral therapy over monitoring alone**
Moderate Risk	**Suggest antiviral therapy over monitoring alone**
Low Risk	**Suggest monitoring alone over antiviral therapy**

Treatment : TDF, TAF, Entecavir
Continue at least 6 months after discontinuation of immunosuppressive therapy
Continue at least 12 months after discontinuation of B-cell depleting therapy

Investigational Therapy

Bepirovirsen: Antisense oligonucleotide (ASO)



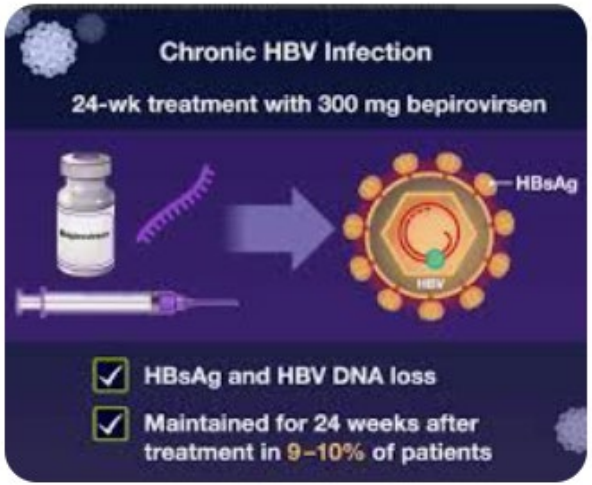
- Modified single strand oligonucleotide
- Targets all HBV RNA sequence
- Significant uptake by non-hepatocyte liver cells like kupfer cells/macrophages resulting in immunostimulatory effect

Virginia Mason Franciscan Health
A member of CommonSpirit

Yuen, M-F et al
N Engl J Med 2022;387:1957-1968

B-Clear _ Bepirovirsen Trial

* Gp 1 -300mgs/weekly SQ 24weeks, gp 2 300mgs for 12 weeks then 150mgs for 12 weeks, Gp 3 300mgs 12 weeks followed by placebo 12 weeks, Gp 4 placebo 12 weeks followed by drug 12 weeks
Weekly subcutaneous injections of Bepirovirsen.



Virginia Mason Franciscan Health
A member of CommonSpirit

Yuen M-F NEJM 2022

B- Sure
Long term followup of B-Clear

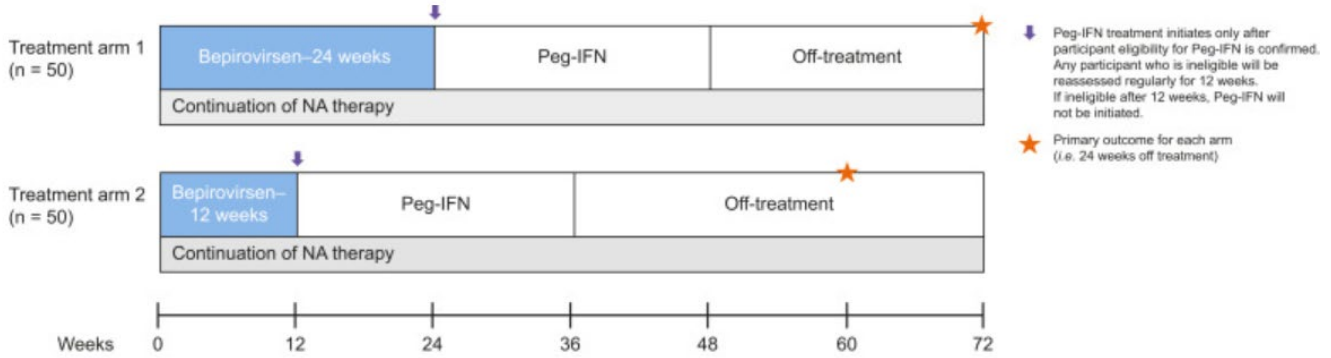
Prospective long term followup study of participants who achieved a complete or partial response in the earlier B-Clear Phase 2b trial.

Aim : assess the long-term durability of the bepirovirsen treatment response, particularly after patients stop all hepatitis B therapy

Interim Analysis - small number of responders have maintained response of long term followup – 3 non-NA patients with ≥9month followup maintained response and 4 NA treated who stopped NAs maintained response

Virginia Mason Franciscan Health
A member of CommonSpirit

B-Together: Sequential Bepirovirsen and PegINF added to NA therapy for Chronic HBV



- 24-week posttreatment response rates 9% - 15% in B-Together vs 3% to 9% in Phase 2B B clear trial of BPV alone for 12-24 weeks in participants receiving stable NA therapy for HBV
- Response rates higher in participants with lower baseline HBsAg levels

Virginia Mason Franciscan Health
A member of CommonSpirit

Buti, Maria et al.Journal of Hepatology, Volume 82, Issue 2, 222 - 234

HBV Treatment Pipeline-Potential Strategies to Achieve Functional Cure

Replication inhibition	±	Antigen reduction	±	Immune modulation
HBV polymerase inhibitor: HS-10234 **Capsid inhibitors:** ALG-000184 ZM-H1505R **HBsAg inhibitor:** REP 2139		**HBsAg release:** REP 2139 **ASO*:** Bepirovirsen AHB-137 **siRNAs*:** AB-729 BW-20507 JNJ-3989 VIR-2218		**TLR agonist:** GS9688 **Various:** ASC22 APG-1387 GSK 4388067A **Monoclonal antibodies:** Burfiralimab VIR-3434

*May also inhibit viral replication.

Virginia Mason Franciscan Health
A member of CommonSpirit

Feld. Clin Gastroenterol Hepatol. 2023;21:2040. hepb.org/treatment-and-management/drug-watch/. Vaillant. Viruses. 2022;14:2052.

Slide credit: clinicaloptions.com

CCO powered by CEA

Simplified Guidelines

Screen all adults with HBV triple test pance

Vaccinate all adults if no immunity

HBsAg+ link to HBV DNA and anti-HDV

Treat all (most) HBV DNA detectable patients

Surveillance for HCC

HDV

HDV - “satellite virus” “incomplete virus”

Can only infect those with HBV

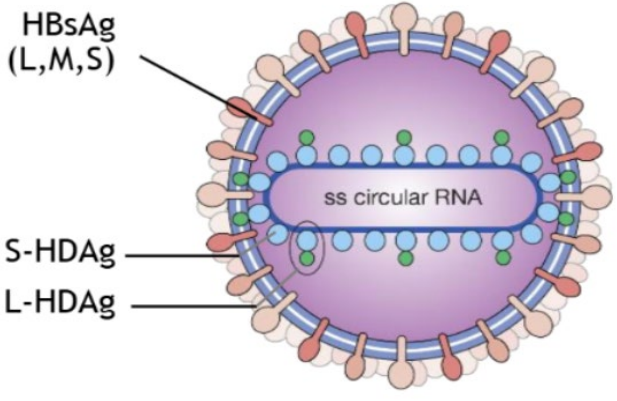
Maybe acquired as a co-infection or superinfection

Among HBsAg positive people, estimated prevalence of HDV is 4.5% (~12 million)

HDV causes rapid progression to cirrhosis and HCC
HBV/HDV co-infected patients 2-fold increased risk of HCC compared to HBV mono-therapy

Test - anti-HDV antibody → confirm with HDV RNA

HDV has an envelope consisting of HBsAg[1]

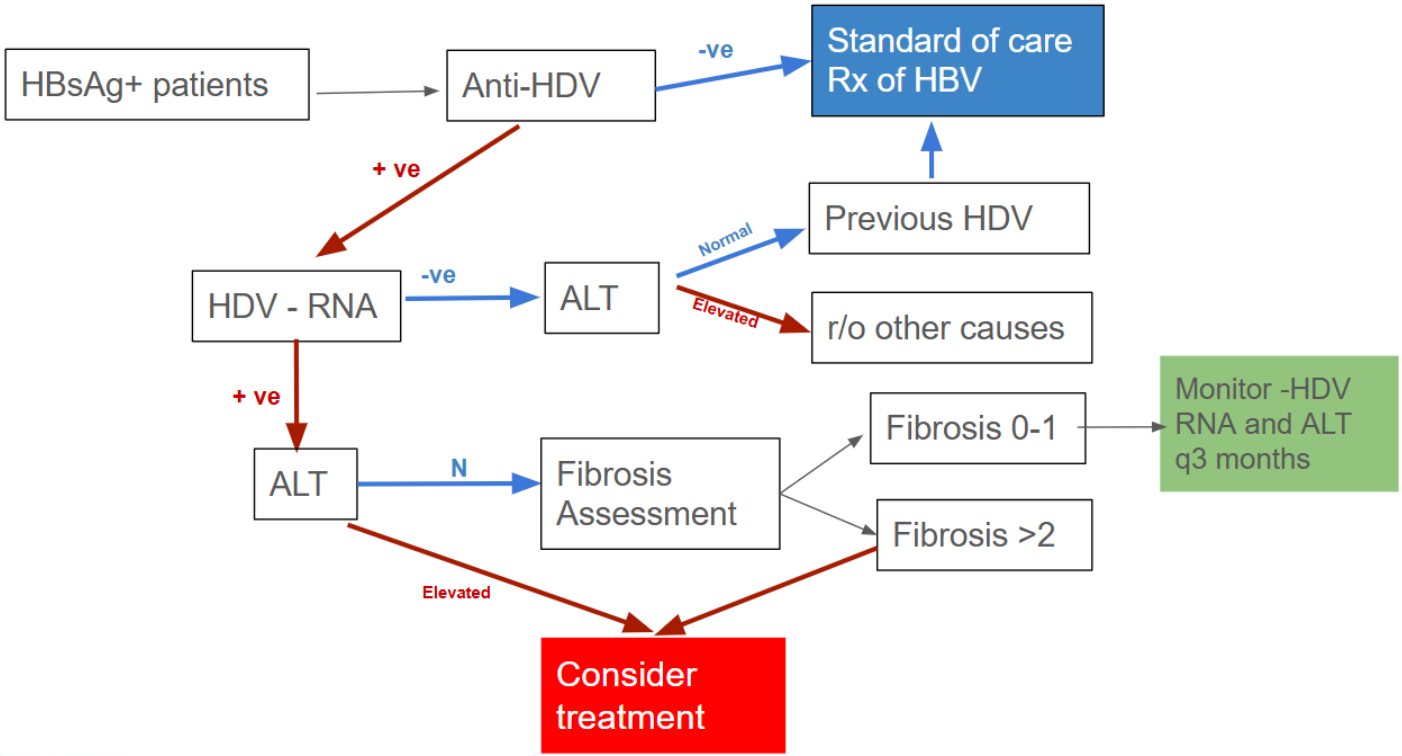


L-HBsAg is required for viral entry into hepatocytes via NTCP transported

Virginia Mason Franciscan Health
A member of CommonSpirit

1. Adapted from Lempp FA, et al. Nat Rev Gastroenterol Hepatol 2016;13:580-9;

Algorithm for HDV Evaluation



Virginia Maso
Franciscan He

Adapted from: Shah. Gastroenterol Rep (Oxf). 2019:7:396.

Treatment HDV

Medication: PegIFN

Duration: 12- 24 months

Virologic response rate: 17-47%

Rate of HDV RNA negativity at 24wk after treatment cessation: 5%

Nucleus(t)ide analogues used to treat HBV is NOT active against HDV

HBV vaccination is best way to prevent HDV

Consider PegIFN in all patients with HDV and compensated liver disease (even in presence of cirrhosis)

HDV EASL Recommendation - Bulevirtide (BLV)

Bulevirtide: HDV/HBV Cell Entry Inhibitor

Disrupts binding of HBV-preS1 to NTCP

Dose: 2mg SC daily

Duration: not yet defined , long-term

Combination with PegIFN maybe considered

BLV is not currently approved in US

Consider BLV in all patients with HDV and compensated liver disease (even in presence of cirrhosis)

Conclusion

Screen all and treat all (aleast most !)

NA’s are highly effective and safe

Expanding treatment will reduce complications such as progression to HCC development

Thank you

Virginia Mason Franciscan Health™
A member of CommonSpirit