Approach to HBV Treatment

KARLA THORNTON, MD, MPH

PROFESSOR, DIVISION OF INFECTIOUS DISEASES, UNMHSC

SENIOR ASSOCIATE DIRECTOR, PROJECT ECHO

Conflicts of Interest Disclosure Statement

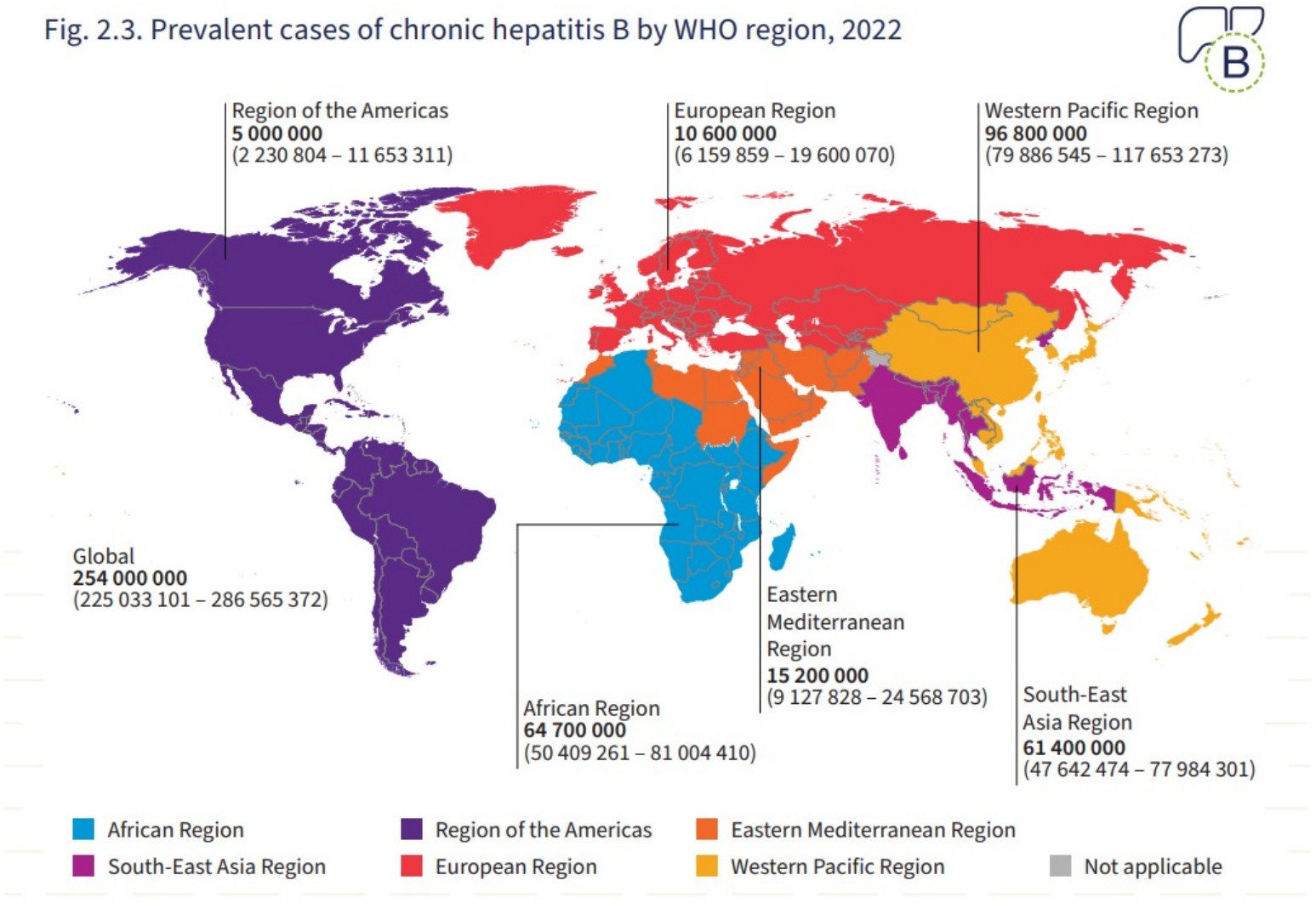
I have no conflicts of interest to disclose.

Learning Objectives

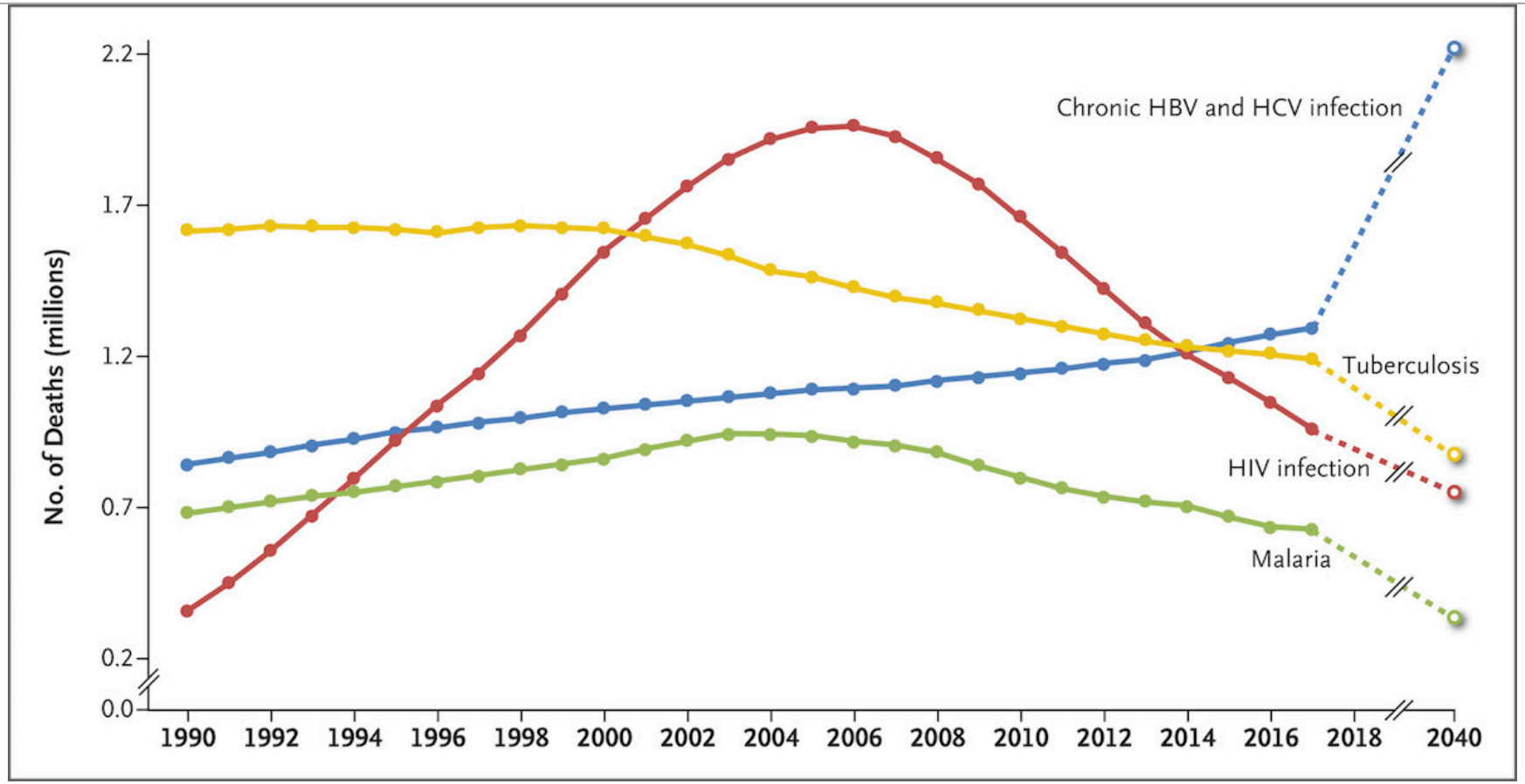
- Identify appropriate baseline serologies for HBV
- Identify who should be offered treatment for HBV
- Recognize the current recommended medications for HBV treatment

Hepatitis B: Global Burden

Fig. 2.3. Prevalent cases of chronic hepatitis B by WHO region, 2022



Global HBV-related Deaths



Thomas DL. Global Elimination of Chronic Hepatitis. N Engl J Med. 2019;380:2041-50.

HBV Awareness

A minority of persons living with chronic HBV are aware of their HBV infection status

NHANES data (2013 through 2016)

- 33.9% of those with chronic infection were aware of their HBV status.
- 11.7% of persons with a past exposure to HBV (defined by the presence of HBcAb) were aware they had been exposed to HBV

Kim HS, Yang JD, El-Serag HB, Kanwal F. Awareness of chronic viral hepatitis in the United States: An update from the National Health and Nutrition Examination Survey. J Viral Hepat. 2019 May;26(5):596-602. doi: 10.1111/jvh.13060. Epub 2019 Mar 13. PMID: 30629790.

CDC Screening and Testing Recommendations for Chronic Hepatitis B Virus Infection (HBV)

(MMWR March 10, 2023)

Summary of 2023 HBV screening and testing recommendations

Screen all adults aged 18 years and older at least once in their lifetime using a triple panel test

Screen pregnant people for hepatitis B surface antigen (HBsAg) during each pregnancy regardless of vaccination status and history of testing

Expand periodic risk-based testing to include people incarcerated, people with a history of sexually transmitted infections or multiple sex partners, and people with hepatitis C virus infection

Test anyone who requests HBV testing regardless of disclosure of risk

https://www.cdc.gov/mmwr/volumes/72/rr/rr7201a1.htm?s_cid=rr7201a1_w –accessed 7_28_23

HBV Testing and Serology Interpretation

HBV Terminology

Name	Abbreviation	Interpretation
Hepatitis B Surface Antigen	**HBsAg**	**Indicates active infection. Indicates chronic infection if persistent >6 mos.**
Hepatitis B Surface Antibody	**anti-HBs**	**Indicates immunity.**
Hepatitis B Core Antibody	**anti-HBc**	**Indicates exposure. NOT seen in those immune because of vaccine.**

HBsAg	Anti-HBs	Anti-HBc	Interpretation
–	–	–	Susceptible. Vaccinate!
+	-/+	+	Chronic infection
–	+	–	Immune from prior vaccination
–	+	+	Exposure with immune control, low risk of reactivation
–	–	+	Exposure with minimal or no immune control, higher risk of reactivation

Hepatitis B Management: Guidance for the Primary Care Provider

Last updated February 24, 2020

The purpose of this document is to provide simplified, up-to-date, and readily accessible guidance for primary care medical providers related to the prevention, diagnosis, and management of hepatitis B virus (HBV) infection, including hepatocellular carcinoma surveillance.

About the HBV Primary Care Workgroup

This guidance was developed by the Hepatitis B Primary Care Workgroup, a multidisciplinary panel of national experts in the field of viral hepatitis B, including representation from hepatology, infectious diseases, pharmacy, primary care, public health, and other national organizations. The workgroup was organized by the National Taskforce on Hepatitis B in partnership with the San Francisco Hep B Free — Bay Area and Project ECHO™ and did not receive any outside funding.

Collaboration with University of Washington

This guidance was produced in collaboration with the University of Washington's National Hepatitis Training Center (HTC). The UW HTC will host and feature the most current version of these guidelines on the free *Hepatitis B Online* website (www.xxxxxx). The UW HTC is funded by the Centers for Disease Control and Prevention (CDC).

Suggested citation. Tang AS, Thornton K, and HBV Primary Care Workgroup. Hepatitis B Management: Guidance for the Primary Care Provider. February 17, 2020. [hepatitisB.uw.edu/hbv-pcw/guidance]

TABLE OF CONTENTS

HBV Primary Care Workgroup

HBV GUIDANCE CO-CHAIRS
Amy S. Tang, MD
Karla Thornton, MD, MPH

HEPATOLOGY
Eric W. Chak, MD, MPH
Robert G. Gish, MD
Anna S. Lok, MD
Brian J. McMahon, MD
Lewis R. Roberts, MB, ChB, PhD
Norah A. Terrault, MD, MPH

INFECTIOUS DISEASES
Camilla S. Graham, MD, MPH
David H. Spach, MD
Mark S. Sulkowski, MD
Karla Thornton, MD, MPH

PHARMACY
Paulina Deming, PharmD

PRIMARY CARE
Richard Andrews, MD, MPH
Amy S. Tang, MD
Grace Wang, MD, MPH
Su Wang, MD, MPH

PUBLIC HEALTH
Moon S. Chen Jr., PhD, MPH
Chari Cohen, DrPH, MPH
Stuart Fong, MD
Aaron M. Harris, MD, MPH
Rita K. Kuwahara, MD, MIH
Richard So, MPH, MPA
Ann Winters, MD

Additional Workgroup Support
Melanie Bird, PhD
Jennifer Lim
Amir Qaseem, MD, PhD
Amy Trang, PhD, M.Ed

Management of the HBsAg (+) Patient

Cirrhosis	HBV DNA (IU/mL)	ALT (U/L)	Management
YES	Any	Any	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Refer to specialist for screening endoscopy and, if needed, for other cirrhosis-related complications > HCC surveillance, including in persons who become HBsAg(-) (page 7) > All patients with decompensated cirrhosis[2] should be promptly referred to a hepatologist
NO	>2,000	Elevated[3]	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Monitor HBeAg and anti-HBe every 6 months in patients who are HBeAg+ at time of treatment initiation to evaluate for seroconversion from HBeAg(+)/anti-HBe(-) to HBeAg(-)/anti-HBe(+) > Check HBsAg annually if/when HBeAg negative
		Normal	> Monitor HBV DNA and ALT every 6 months > Liver fibrosis assessment every 2 to 3 years
	≤2,000	Elevated[3]	> Evaluate other etiologies for elevated ALT > Monitor HBV DNA and ALT every 6 months
		Normal	> Monitor HBV DNA and ALT every 6 months and HBsAg every 1 year for seroclearance

Preferred Antiviral Treatment of the HBsAg (+) Patient

Drug	Adult dose	Pregnancy category[1]	Side effects	Monitoring on treatment
Entecavir *Baraclude*	Standard: 0.5 mg by mouth daily Decompensated liver disease: 1 mg by mouth daily Take 2 hours before or after food	Formerly FDA category C Limited pregnancy exposure, pregnancy exposure registry available Insufficient human data to assess risk of major birth defects No adverse effects observed in animal studies	Headache, fatigue, dizziness, nausea reported in ≥3% Post-marketing surveillance include infrequent reports of: > lactic acidosis > severe hepatomegaly	Adjust dose with CrCl <50 mL/min Avoid in pregnant patients Avoid in patients with prior exposure to lamivudine or known lamivudine resistance Lactic acid levels if clinical concern

Preferred Antiviral Treatment of the HBsAg (+) Patient

Drug	Adult dose	Pregnancy category[1]	Side effects	Monitoring on treatment
Tenofovir disoproxil fumarate (TDF) *Viread*	300 mg by mouth daily Take without regard to food	Formerly FDA category B Pregnancy exposure registry available Extensive data from pregnant women with HIV or HBV infections indicate no increase in pregnancy complications or major birth defects	Nausea (9%) Post-marketing surveillance include infrequent reports of: > nephropathy > Fanconi syndrome > osteomalacia > lactic acidosis	Adjust dose with CrCl <50 mL/min Serum creatinine at baseline; if at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein at least annually Consider bone density study at baseline and during treatment in persons with history of fracture or risks for osteopenia Lactic acid levels if clinical concern
Tenofovir alafenamide (TAF) *Vemlidy*	25 mg by mouth daily Take with food	No human data in pregnancy No adverse effects observed in animal studies	Headache (12%) Lactic acidosis/ severe hepatomegaly with steatosis is a warning for tenofovir AF due to rare reports with use of tenofovir DF	Avoid with CrCl <15 mL/min if not receiving hemodialysis Dose after HD in those on HD If at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein as clinically indicated. Lactic acid levels if clinical concern

Key Points

HBV is a major global health problem

Screen all adults 18 years or older with the triple panel

HBcAb indicates exposure to HBV

HBsAg indicates active HBV infection

Decision to treat based on HBVDNA level and degree of liver inflammation

Treat all patients with cirrhosis

Treat pregnant women in 3rd trimester at risk of transmission

HBV is **not curable** (with current treatment) but is controllable with improved patient outcomes

Resources

https://www.cdc.gov/hepatitis/

https://www.hepatitisb.uw.edu/

Hepatitis B Management: Guidance for the Primary Care Provider - HBV Primary Care Workgroup - Hepatitis B Online (uw.edu)

WHO Global Hepatitis report: https://www.who.int/publications/i/item/9789240091672

Questions?