Managing Hepatitis B Care for High Risk African and Caribbean Populations

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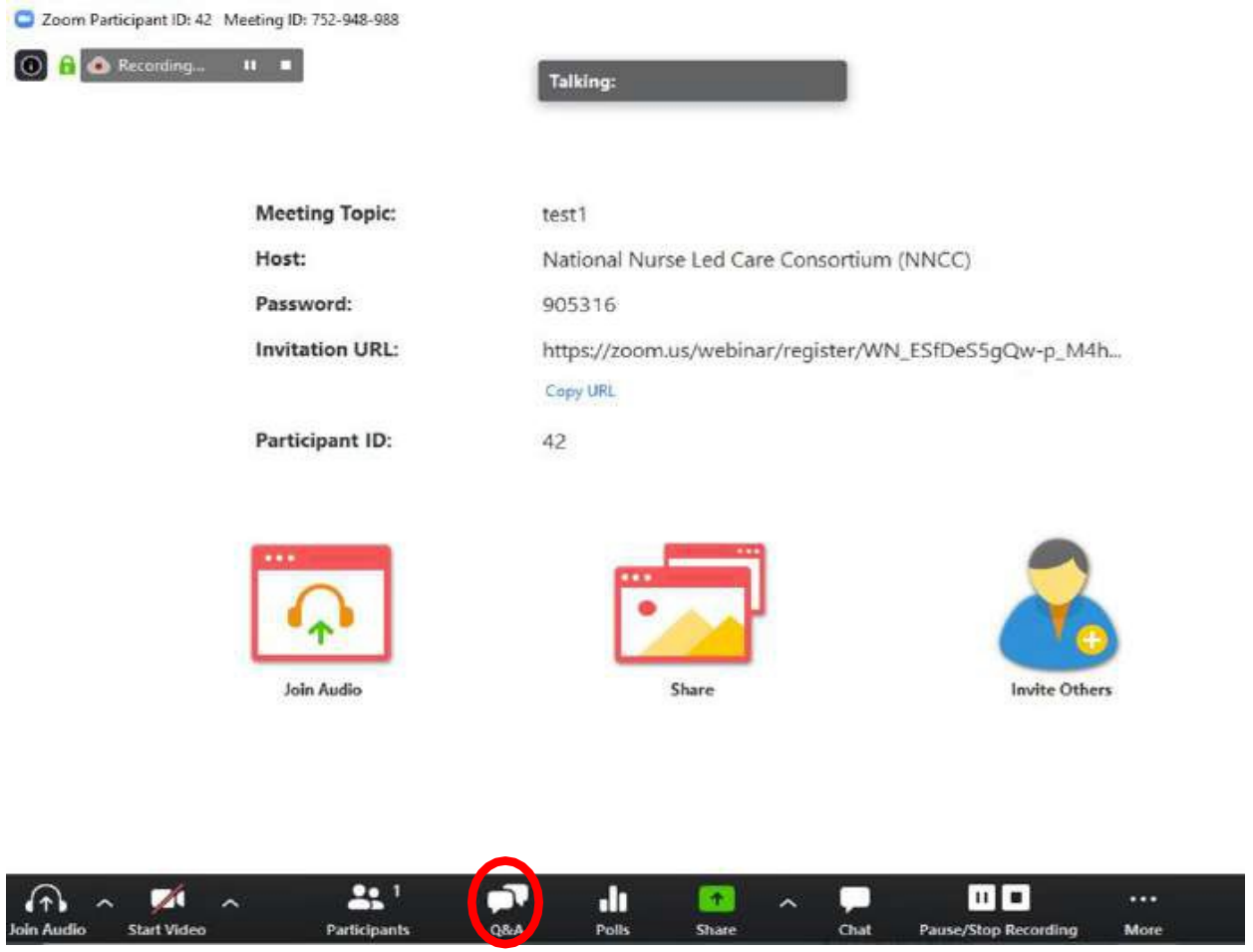


Managing Hepatitis B Care for High Risk African and Caribbean Populations

Eyob L. Feyssa, MD, MPH, FACP, FAASLD.
Associate Professor of Medicine
Center for Liver Disease
Tower Health Transplant Institute

Disclosure of Conflicts of Interest

- **Eyob L. Feyssa, MD, MPH, FACP, FAASLD,** has affiliations with Gilead Sciences and Abbvie (*Speakers Bureau*);

- I have NOT included discussion on unlabeled uses of a commercial product or an investigational use of a product not yet approved for this purpose

Learning Objectives

- Demonstrate Hepatitis B knowledge and review current epidemiological and behavioral risk trends for African and Caribbean immigrant population

- Provide guideline-based recommendations on screening and treating patients with Hepatitis B infection

- Review evidence of benefits of antiviral therapy and associated reduction of HCC risks.

Introduction

- Hepatitis B
  - DNA virus
  - Blood born transmission
    - Sexual contacts
    - Vertical / Perinatal transmission
    - Injection drug use
    - Other percutaneous or mucosal exposure, e.g. Tattoos
  - Varied clinical presentation
    - Asymptomatic
    - Acute infection
    - Chronic infection
    - Risk of cirrhosis and liver cancer

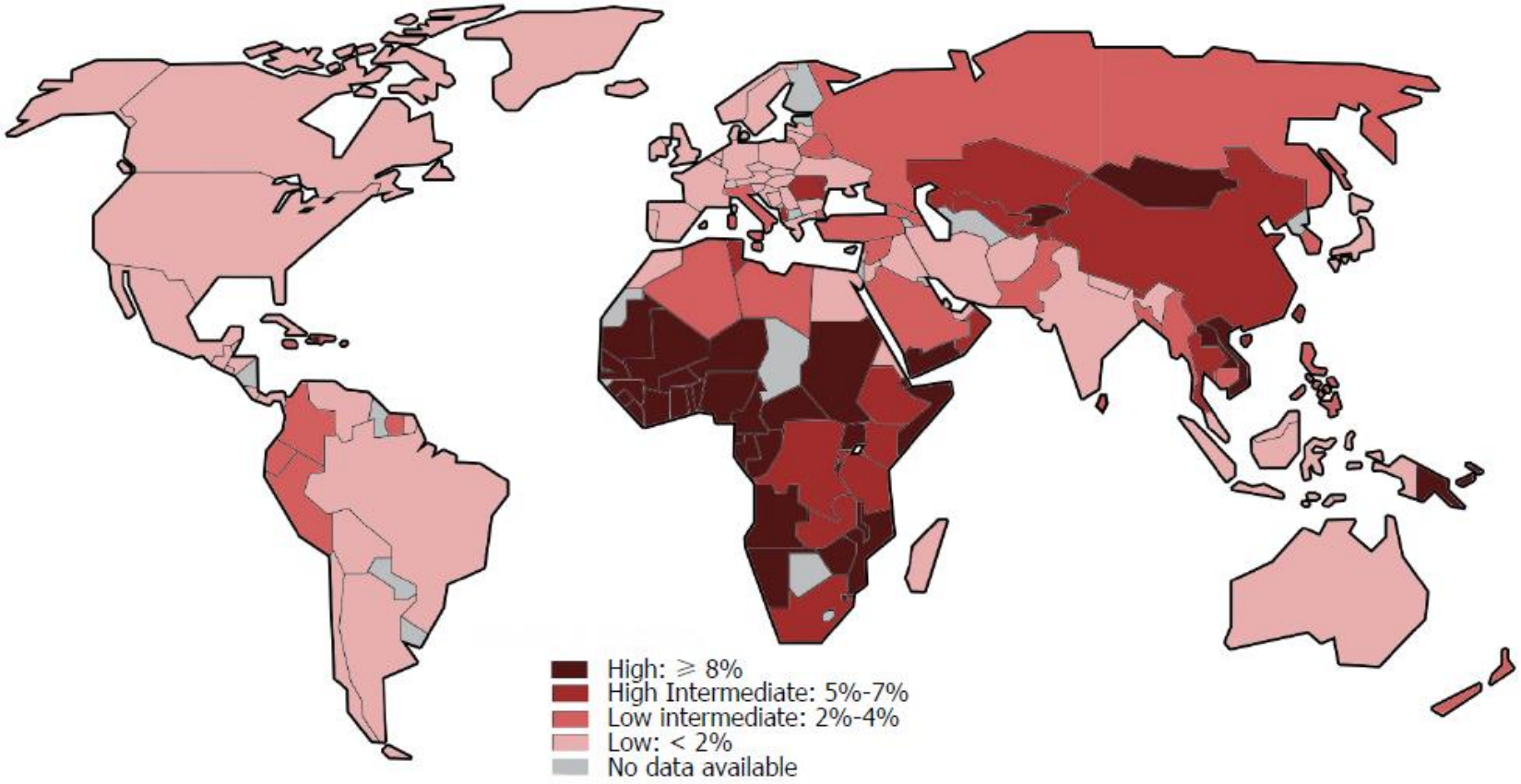
- Worldwide about 257 million people had hepatitis B infection.

Hepatitis B Infection: Epidemiology and burden of disease

Prevalence of Hepatitis B Virus Infection

Screen for HBV infection based on geographic distribution:

- **Patients born in areas of intermediate and high HBV prevalence**
- **Patients born in US to parents from areas of high HBV prevalence**



Source: Schweitzer A, Horn J, Mikolajczyk R, Krause G, Ott J. Estimations of worldwide prevalence of chronic heptitis B virus infection: a systematic review of data published between 1965 and 2013. The Lancet. 2015 Jul 28; 386(10003): 1546-1555.

Hepatitis B prevalence

Hepatitis B Virus Infection in African Countries

- Prevalence
  - More than 75 million people with HBV in African continent
  - Prevalence of HBV infection varies among African countries (? Lack of adequate data)
    - South Sudan, Liberia, Guinea: ≥15%
    - Nigeria, Senegal, Somalia, Zimbabwe: 9.8%-14.8%
    - Eritrea, Ethiopia: 2.5%-6.0%

- HBV is more sever in Africa
  - Liver cancer is the 3rd most common cancer in Africa
  - HBV is a leading risk factor for Liver Cancer
    - Up to 65% of liver cancer could be attributed to HBV infection

Schweitzer A, et al. *Lancet.* 2015;386:1546-1555.
Sylla BS, Wild CP. Int J Cancer. 2012;130:245-250.
Kew MC. World J Hepatol. 2010;2:65-73.
de Martel C, et al. Hepatology. 2015;62:1190-1200

Hepatitis B Virus Infection in Caribbean Countries

- > 1 million people with HBV infection currently live in Caribbean countries
- Estimated prevalence of HBV infection
  - Haiti has the highest prevalence rate (13.6%)
  - Dominican Republic (4.1%)
  - Jamaica (3.8%)
- High liver cancer related mortality in men attributed to HBV infection

1. Schweitzer A, et al. *Lancet.* 2015;386:1546-1555.
2. International Agency for Research on Cancer. GLOBOCAN 2012 Data. http://globocan.iarc.fr/Default.aspx. Accessed October 20, 201

Hepatitis B Virus Infection in US

- Estimated 2 million people in US have HBV
  - Majority are are foreign-born (1.6 million people)
  - High HBV prevalence in African and Caribbean immigrants in the US
    - African immigrants 10.3%
    - Caribbean Immigrants 4.5%

- Most people with HBV in US undiagnosed
  - 70% of people are unaware of their HBV infection
  - At risk for advanced liver disease and liver cancer

- Even from those who are diagnosed with HBV, only small proportion are in care and received treatment (2.5%)

1. Cohen C, et al. *J Viral Hepat*. 2011;18:377-383.
2. Keeffe EB, et al. *Clin Gastroenterol Hepatol*. 2008;6:1315-1341.
3. Kowdley KV, et al. *Hepatology*. 2012;56:422-433.
4. US Census Bureau. *The Foreign-Born Population From Africa: 2008-2012.* October 1, 2014. www.census.gov/library/publications/2014/acs/acsbr12-16.pdf. Accessed October 20, 2015.
5. Kowdley KV, et al. *Hepatology*. 2012;56:422-433.

Hepatitis B Infection: Transmission and Natural History

Routes of HBV Transmission

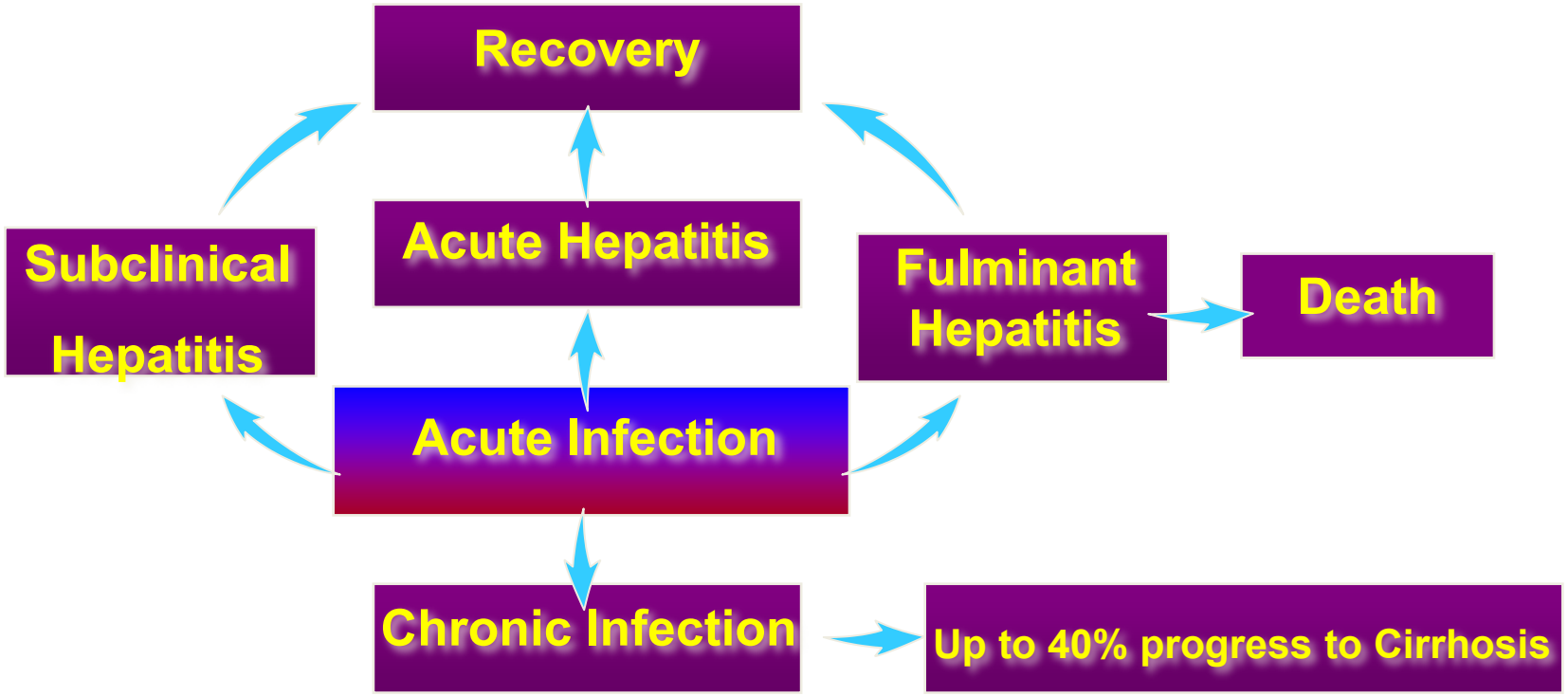
- Vertica transmission
  - Up to 90% infants born to HBV infected mother could develop HBV infection.

- Prolonged / household contact

- Exposure to infected blood or body fluid
  - Sexual contacts of HBV infected person
  - Injection drug use
  - Hemodialysis
  - Transfusion or organ transplant from infected donor
  - Nonsterile tattooing and body piercing needles

1. CDC. *Morb Mortal Wkly Rep.* 2008;57:1-20.
2. Buchanan C, Tran TT. *Clin Liver Dis.* 2010;14:495-504.

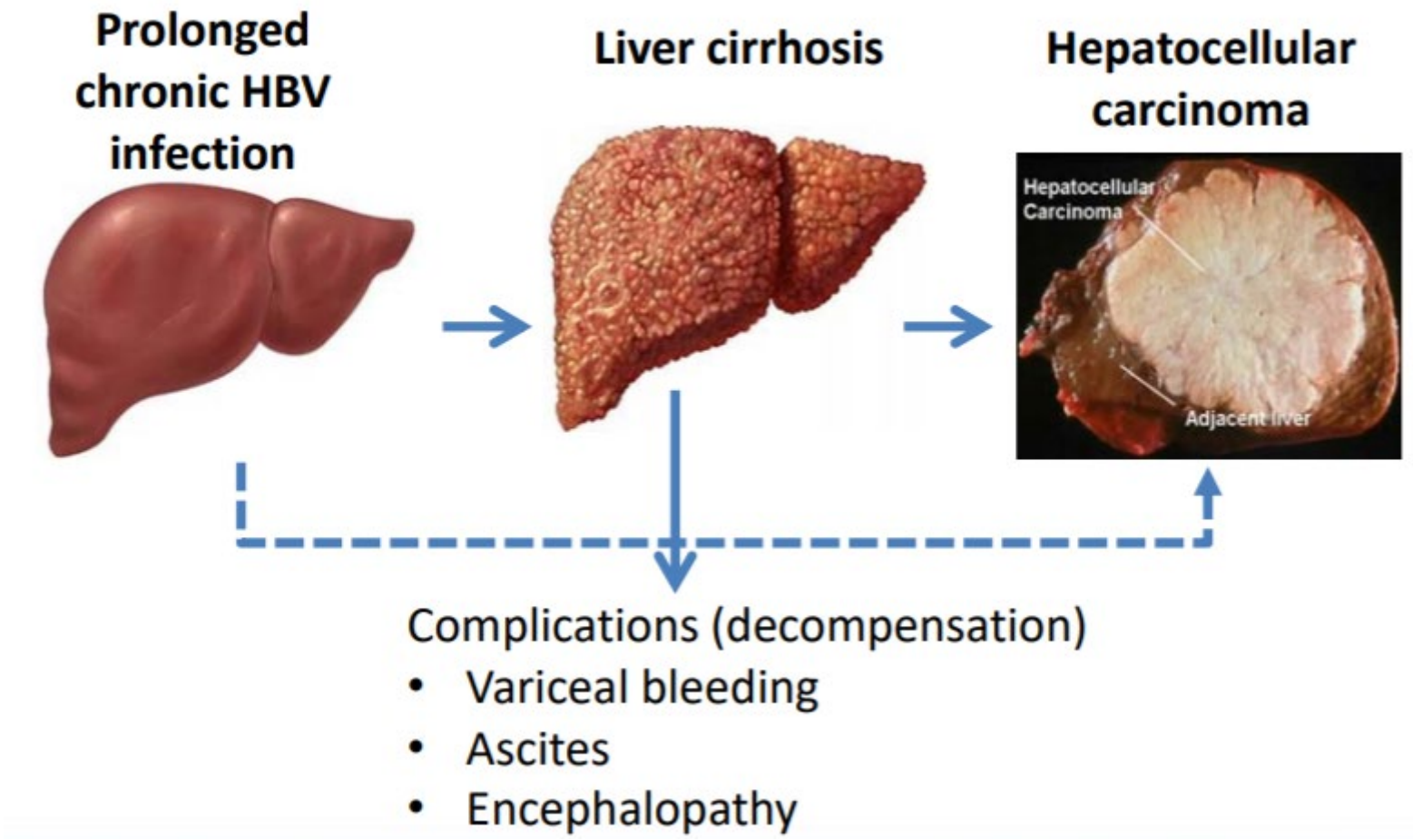
HBV Disease Progression



Progression to HBV-related complications depends on a combination of host and viral factors

1. WHO. *Wkly Epidemiol Rec.* 2009;94:405-420. 2. Hyams KC. *Clin Infect Dis.* 1995;20:992-1000. 3. Torresi J, Locarnini S. *Gastroenterology.* 2000;118 (2 suppl 1):S83–S103. 4. Sarin SK, Kumar M. In: Shetty K, Wu GY (eds). *Clinical Gastroenterology: Chronic Viral Hepatitis.* 2009; Totowa, NJ: Humana Press; 185-241. 5. Fattovich G, et al. *Gastroenterology.* 2004;127(5 suppl 1):S35-S50. 6. Keeffe EB, et al. *Clin Gastroenterol Hepatol.* 2008;6:1315-1341. 7. Cohen-Naftaly M, Friedman SL. *Ther Adv Gastroenterol.* 2011;4:391-417. 8. Chen CJ, et al. *JAMA.* 2006;295:65-73. 9. Iloeje UH, et al. *Gastroenterology.* 2006;130:678-686.

Liver related complications of HBV infection



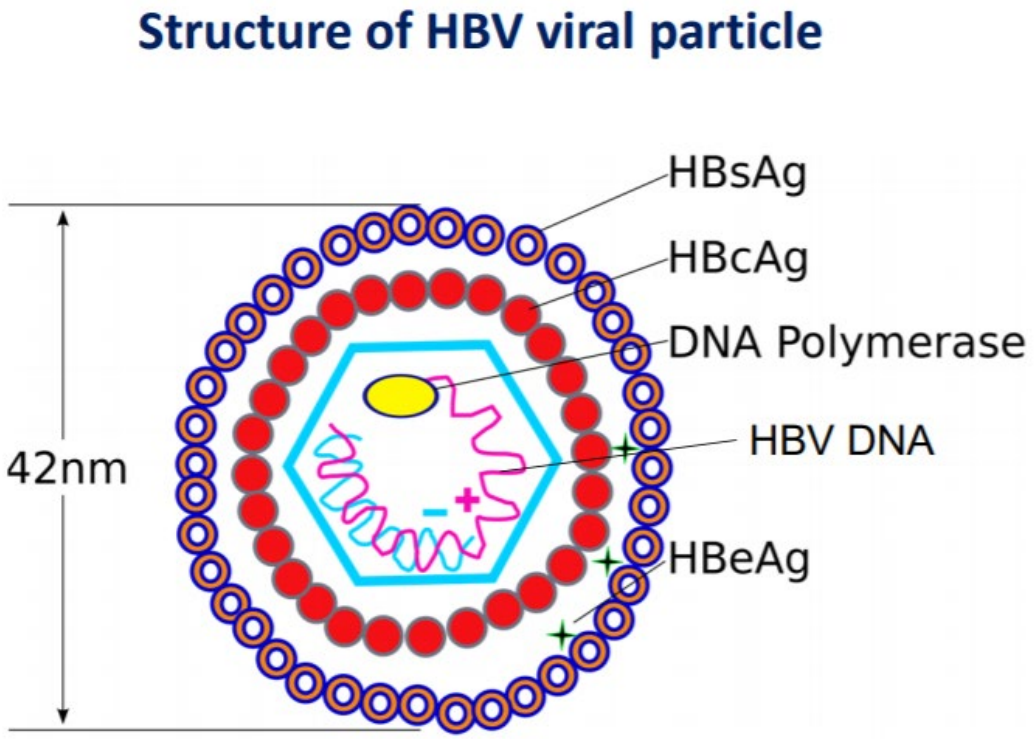
Cirrhosis is a strong risk factor for HCC. However, HCC associated with HBV occurs in the absence of cirrhosis (30-50% of cases).

Lok ASF, McMahon BJ. *Hepatology*. 2009;50:1-36.

Hepatitis B Infection: Serologic markers and diagnosis

Serologic Markers in HBV Infection

- HBsAg
  - Hallmark of HBV infection
- Anti-HBs
  - Antibody to HBsAg
  - Marker of recovery and immunity
- Anti-HBc
  - Antibody to HBV core antigen
  - Marker of prior exposure (IgM recent / acute)
- HBeAg
  - Usually associated with active replication
  - Indicates higher infectivity
- HBV DNA (viral load)
  - indicates ongoing viral replication
  - Marker of infectivity and risk of major liver disease



Interpretation of HBV infection Serologic Results

HBsAg	Total Anti-HBc	IgM Anti-HBc	Anti-HBs	Interpretation
Negative	Negative	--	Negative	Susceptible; offer vaccination
Negative	Positive	--	Positive	Immune due to natural infection
Negative	Negative	--	Positive	Immune due to hepatitis B vaccination
Positive	Positive	Negative	Negative	**Chronic HBV infection**
Positive	Positive	Positive	Negative	**Acute HBV infection**
Negative	Positive	--	Negative	Unclear; could be any one of the following: 1. Resolved infection (most common) 2. False-positive anti-HBc; susceptible 3. “Low-level” chronic infection 4. Resolving acute infection

CDC. Hepatitis B FAQs for Health Professionals.

Hepatitis B Infection: Management

Interventions to manage HBV infection

- Screen at-risk patients
- Vaccinate those who are unprotected
- Identify and evaluate patient who are positive for HBV infection
  - Evaluate for degree of liver disease
  - Evaluate for treatment
  - Screen and surveillance for liver cancer
  - Regular follow up
- Counsel patient and preventive measures

HBV Screening Recommendations in High-Risk Individuals

- People born in regions where the prevalence of HBV infection is ≥2%
- US-born people not vaccinated as infants and whose parents were born in regions having an HBV prevalence of ≥8%
- Household and sexual contacts of persons with HBV infection
- All pregnant women
- Men who have sex with men
- Injection drug users
- Individuals infected with HCV or HIV
- People with certain medical conditions
  - Needing immunosuppressive therapy
  - Undergoing hemodialysis
- People with elevated ALT or AST of unknown etiology
- People with risk of exposure
  - Donors of blood/organ/tissue
  - Healthcare providers
  - People exposed to bodily fluids
  - People who are incarcerated

https://hepbmd.com/hepatitis-b-risk
CDC. *Morb Mortal Wkly Rep*. 2008;57:1-20.
Lok ASF, McMahon BJ. *Hepatology*. 2009;50:1-36.
USPSTF. Consumer Fact Sheet. May 2014. www.uspreventiveservicestaskforce.org/uspstf12/hepb/hepbrecfact.pdf.

Vaccination of susceptible Individuals

- Definition of protective response
  - Anti-HBs >10 IU/L

- Prevention of infection
  - Pre-exposure
    - Immunocompetent adults and children >95%
  - Post-exposure
    - Infants born to HBsAg + mothers
      - Vaccine alone 65%-95%
      - Vaccine + HBIG 85%-95%

Example of HBV vaccination schedule

U.S. Children and Adult Hepatitis B Vaccine Schedules

For children ≥ 1 and adults

Vaccine	Dose 1	Dose 2	Dose 3
3-dose vaccine series Brand names: Engerix-B, Recombivax HB, Twinrix (hepatitis A and B)	Now ✓	1 month after dose 1 ✓	6 months after dose 1 ✓
2-dose vaccine series Adults ≥ 18 Years Brand name: Heplisav-B	Now ✓	1 month after dose 1 ✓	

Key

✓ = Monovalent hepatitis B vaccine (protection against hepatitis B only)

= Approved for adults

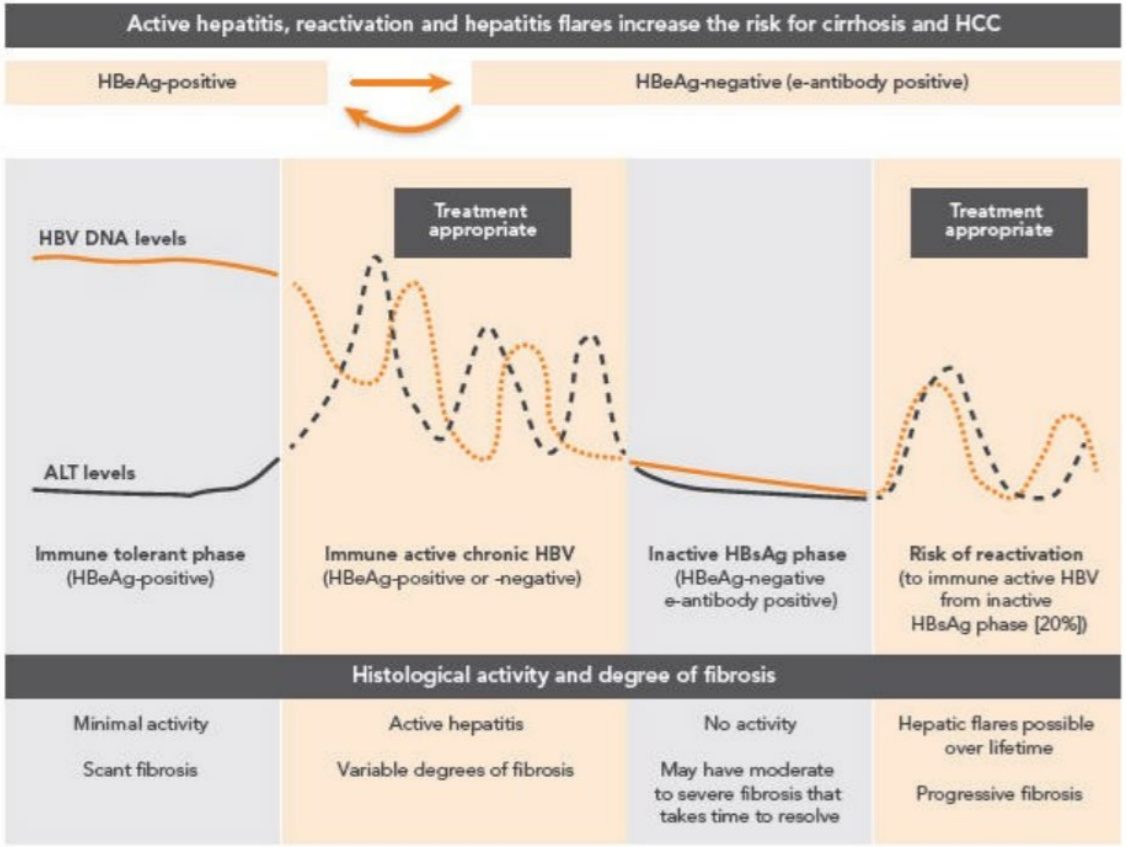
= Approved for children

https://www.hepb.org/prevention-and-diagnosis/vaccination/guidelines-2/

Evaluation of Chronic HBV and Treatment Consideration

- Evaluate HBV activity and liver damage
  - Hepatic panel including ALT
  - HBV DNA viral load
  - HBeAg and Anti-HBeAg status
  - Noninvasive liver fibrosis assessment
  - Liver biopsy may not be necessary
- Screen for liver cancer
  - Ultrasound of liver (+/- AFP) is good screening test
- Evaluate for comorbid conditions
  - Rule out other causes of chronic liver disease
    - HCV, HAV, alcoholic liver disease, NASH etc
    - Screen for HDV
      - HBV/HDV associated with higher risk of cirrhosis, decompensation and HC
  - Bone health, renal function
- Evaluate for antiviral therapy
- Establish long-term follow up
  - HCC surveillance every 6 months
  - Follow up LFTs and HBV DNA
- **Screen household and sexual contacts of persons with HBV infection**

Chronic HBV Treatment Considerations



- HBV is a lifelong and dynamic disease and changes over time
- Risk of end stage liver disease and cancer increases with ongoing inflammation and viremia in adults
- HBV can be controlled but not cured
- Reactivation can occur even in those who have lost HBsAg

https://www.who.int/docs/default-source/searo/hiv-hepatitis/training-modules/07-hbv-natural-history.pdf?sfvrsn=520b7c01_2

Approved HBV treatments over the years

- Interferon alfa-2b – 1991
- Lamivudine – 1998
- Adefovir – 2002
- Entecavir – 2005
- Peginterferon alfa-2a – 2005
- Telbivudine – 2006
- Tenofovir - 2008
- Tenofovir alafenamide (TAF) 2016
  - Novel, Targeted prodrug of Tenefovir
  - 25 mg daily dosing vs TDF 300 mg daily
    - Bone and Renal safety has been explored in registration trials.

Chronic HBV treatment guideline and algorithms

HBeAg+		HBeAg–	
HBV DNA (IU/mL)	**ALT (U/L)**	**HBV DNA (IU/mL)**	**ALT (U/L)**
AASLD 2015[1] >20,000	**AASLD 2015[1] >2x ULN[a] or noninvasive test/ biopsy (+)[b]**	**AASLD 2015[1] >2000**	**AASLD 2015[1] >2x ULN[a] or noninvasive test/ biopsy (+)[b]**
US Treatment Algorithm 2015[2] ≥2000	**US Treatment Algorithm 2015[2] >ULN[a] or** TE*/biopsy (+)[b]	**US Treatment Algorithm 2015[2] ≥2000**	**US Treatment Algorithm 2015[2] >ULN[a] or** TE*/biopsy (+)[b]
EASL 2012[3] >2000	**EASL 2012[3] >ULN[c] and evidence of liver disease[d]**	**EASL 2012[3] >2000**	**EASL 2012[3] >ULN[c] and evidence of liver disease[d]**

aULN for US Treatment Algorithm (2015) and AASLD (2015): 30 U/L (men) and 19 U/L (women).
bNoninvasive testing/TE or liver biopsy showing significant histologic disease.
cULN for EASL (2012) is 40 U/L. In patients with normal ALT, treatment may be considered if HBV DNA >2000 IU/mL and signs of liver disease.
dModerate to severe active necroinflammation and/or at least moderate fibrosis demonstrated with liver biopsy (or non-invasive markers once validated in HBV-infected patients).

EASL=European Association for the Study of the Liver; *TE=transient elastography; ULN=upper limit of normal.

1. Terrault NA, et al. *Hepatology.* 2015 Nov 13. [Epub ahead of print].
2. Martin P, et al. *Clin Gastroenterol Hepatol.* 2015;13:2071-2087.
3. EASL. *J Hepatol.* 2012;57:167-185.

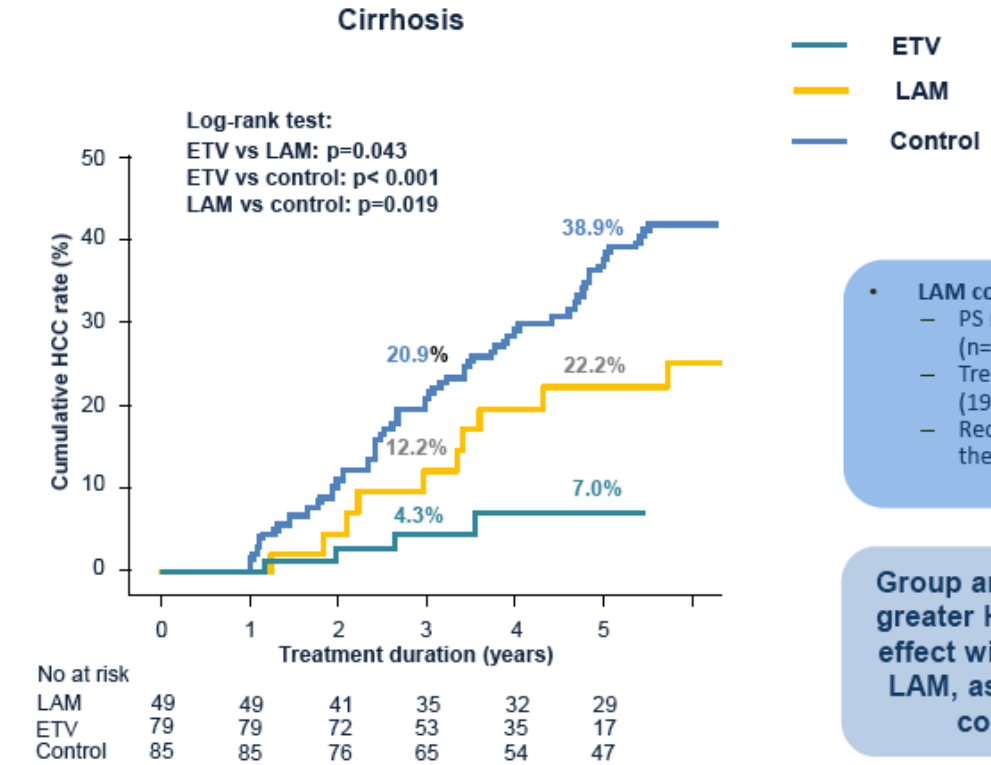
Chronic HBV treatment guideline and algorithms

- Current Viral suppression therapy
  - Who: Treatment of selected patients
    - Active HBV defined by viral load and / or inflammatory activity
    - Cirrhosis
    - Family Hx of HCC
    - Transplant / immunosuppression / Chemotherapy
    - Co-infections
  - Goal: Viral (HBV DNA) suppression on Rx
  - Duration: Long-term therapy, may be indefinite
    - Overtime regression of fibrosis, reduction of HCC risk, improve survival

Chronic HBV treatment reduces HCC incidence

Long-term ETV treatment reduces HCC incidence in patients with HBV infection

HCC incidence lower with ETV than with LAM

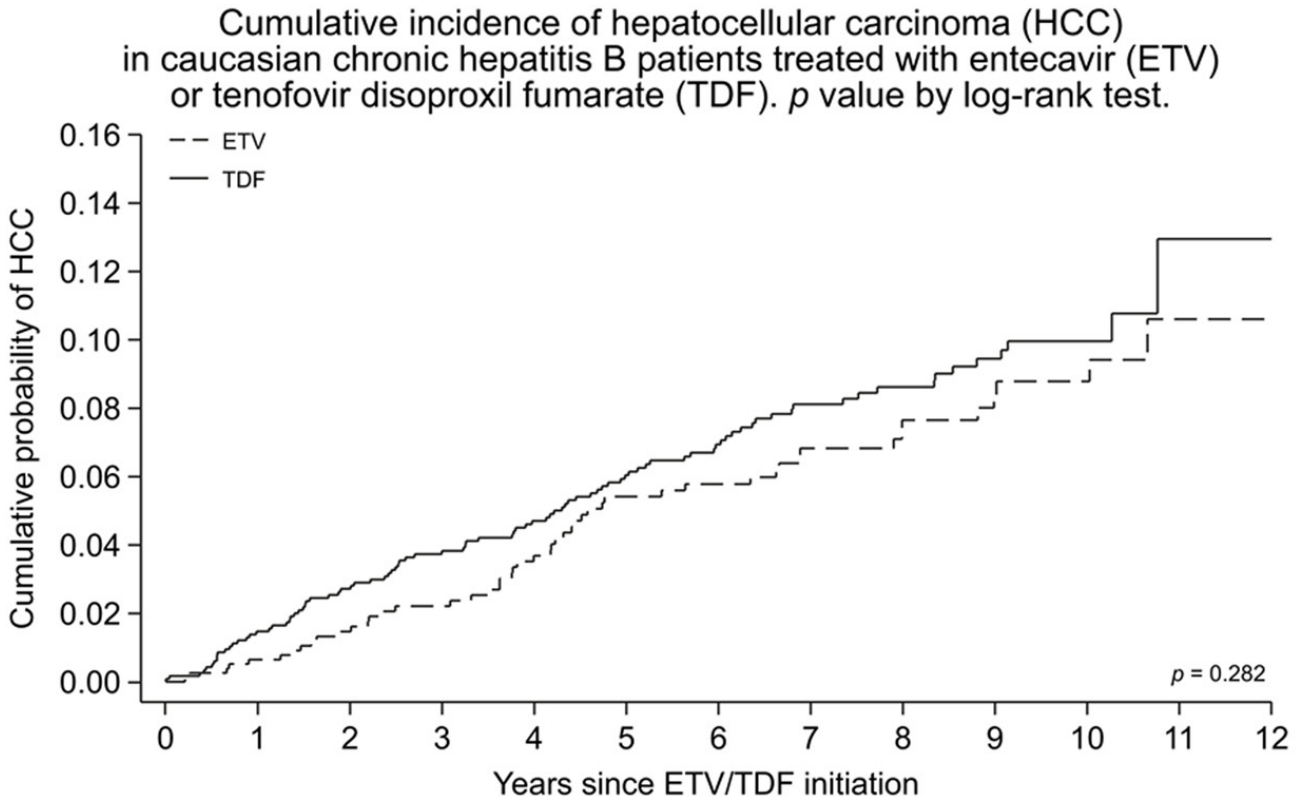


- **LAM cohort:**
  - PS matched LAM cohort (n=182)
  - Treated with LAM (1995–2007)
  - Received no rescue therapy if LAM failure

Group analysis showed a greater HCC suppression effect with ETV than with LAM, as compared with control group

Hosaka T, et al. *Hepatology* 2013

Chronic HBV treatment reduces HCC incidence



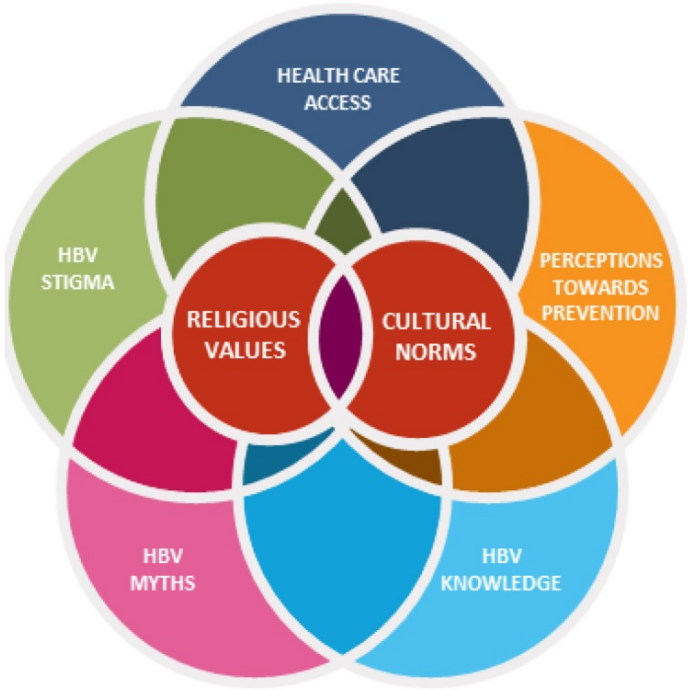
N° at risk													
ETV	772	763	675	618	574	524	492	425	329	238	148	55	7
TDF	1,163	1,125	1,076	1,014	959	883	767	621	499	374	180	36	17

Papatheodoridis GV, et al Similar risk of hepatocellular carcinoma during long-term entecavir or tenofovir therapy in Caucasian patients with chronic hepatitis B. J Hepatol. 2020 Nov;73(5):1037-1045. doi: 10.1016/j.jhep.2020.06.011. Epub 2020 Jun 16. PMID: 32553667.

Hepatitis B Infection: Barriers to care

Barriers to HBV screening and care in the African and Caribbean communities

- Patient Barriers
  - Lack of disease awareness
  - Cultural beliefs and misinformation
  - Religious values
  - Lack of trust in modern medicine
  - Preference for alternative care
  - Fear of Stigmatization
  - Cost of care
- HCP Barriers
  - Lack of who should be screened
  - Language barriers
- Other factors
  - Lack of access to preventive care
  - Lack of insurance
  - Barriers accessing health system
  - Lack of social support



Freeland C, Bodor S, Perera U, Cohen C. Barriers to Hepatitis B Screening and Prevention for African Immigrant Populations in the United States: A Qualitative Study. Viruses. 2020 Mar 11;12(3):305. doi: 10.3390/v12030305. PMID: 32168926; PMCID: PMC7150884.
Francesco F, et al. Hepatitis B Knowledge, Attitudes, and Susceptibility in an Immigrant Caribbean Community. American Journal of Gastroenterology: September 2008 Volume 103 - Issue - p S134

Conclusion

- The prevalence of HBV infection is higher in African and Caribbean immigrants in the US
- Majority of people with HBV in US are undiagnosed and are unaware of their HBV infection
- The current guideline recommends screening for HBV in high-risk population including
  - people born in regions with prevalence of HBV infection > 2%
  - US-born people not vaccinated as infants and whose parents were born in regions having an HBV prevalence of ≥8%
  - Household and sexual contacts of persons with HBV infection

Conclusion

- Chronic HBV infection could lead to cirrhosis, decompensated liver disease and development of hepatocellular carcinoma (HCC).
- HBV infection preventable with effective vaccination in susceptible individuals.
- In patients with chronic HBV, primary goal of therapy is viral suppression.
- Lack of disease awareness and fear of stigmatization are barriers to HBV care in high-risk communities.

Thank You.

Questions?

Please type your questions into the Q&A box.

Christine Simon
csimon@phmc.org

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