Disclosures

- No Disclosures
About Empire Liver Foundation and NYC Health Department

The Empire Liver Foundation is an association of NYS liver specialists dedicated to increasing community awareness of liver disease, providing education on liver disease to health care providers and patients and providing guidance to those who make policy decisions influencing the practice and science of liver disease.

- CME Grand Rounds
- CME Clinical Training Series
- Live Preceptorship
- Mentoring

www.empireliverfoundation.org

The New York City Health Department Viral Hepatitis Program conducts surveillance and develops and implements programs to build capacity to prevent, manage and treat hepatitis B and C in New York City.

- Surveillance
- Community Coalitions
- Navigation Programs
- Clinical Practice Facilitation
- Training

www.HepFree.NYC
Learning Objectives

By the end of this presentation, participants will be able to:

• Describe the epidemiology of HIV/HBV co-infection
• Understand the impact of HIV/HBV co-infection in disease progression and liver-related mortality
• Review the key steps in HIV/HBV co-infection pre-treatment evaluation and treatment
• Review treatment regimens for patients with HIV/HBV confection
• Review Liver cancer screening
Epidemiology
Epidemiology of HBV Infection

- In 2014, WHO estimated 240 million people were chronically infected with HBV.
• In 2014, WHO estimated 35 million people were infected with HIV.
  – 2 to 4 million people are estimated to be HIV/HBV co-infected
  – Sub-Saharan Africa and Asia has the highest rate of HIV/HBV coinfection

Transmission

- HIV and HBV have similar routes of transmission
- Population groups with greatest prevalence of coinfection
  - MSM
  - Injection drug users
  - Patients coming from HBV endemic areas (eg, Sub-Saharan Africa, Asia)

<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>HBV</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Perinatal</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Sexual</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Unsafe injections</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Needlesticks</td>
<td>+++</td>
<td>&lt;+</td>
</tr>
</tbody>
</table>

Sherman KE, et al. Epidemiology, clinical manifestations, and diagnosis of hepatitis B in the HIV-infected patient. In: UpToDate, Mitty J (Ed), UpToDate, Waltham, MA. (Accessed on February 24, 2017.)
1. HIV has been shown to directly infect hepatocytes, hepatic stellate cells (HSC) or Kupffer cells
2. HBV only infects hepatocytes
3. HIV can also significantly impair the integrity of the gastrointestinal tract leading to elevated levels of LPS. LPS can directly activate Kupffer cells and HSC leading to increased intrahepatic inflammation and fibrosis
4. In HBV infection, liver disease can also be mediated by migration from the blood to the liver of HBV-specific and non-HBV specific T cells, chemokine (C-X-C motif) receptor (CXCR) 6 and NK cells [by chemokine (C-X-C motif) ligand (CXCL)10 and CXCL16, respectively] and monocytes [by C-C motif ligand (CCL) 2

Singh et al. AIDS 2017, 31:2035–2052
Impact of HIV on HBV Natural History

- Increases risk of
  - Cirrhosis
  - Hepatocellular carcinoma
  - ESLD related to chronic HBV
  - Death
  - HBV reactivation in inactive carriers
- Lower rate of spontaneous HBeAg or HBsAg seroconversion

Impact of HBV on HIV Natural History

- HBV infection does not
  - Substantially alter HIV progression
  - Influence HIV suppression or CD4 counts following ART initiation

- HIV coinfection adversely affects the natural history of HBV infection at every stage and accelerates the progression of HBV disease.
- However, the impact of HBV in the natural history of HIV does not appear to be significant.

Sarin SK et al. APASL Guideline. Hepatol Int. 2015.
Multicenter, prospective cohort study of liver-related mortality with HBV and HIV infection among 5,622 men followed for a median of 10.5 years (7.5–15.2).

Liver-Related Mortality per 1,000 Person Years in Monoinfected and HIV/HBV Coinfected Patients

- HIV- / HBV-: 0
- HIV- / HBV+: 0.8
- HIV+ / HBV-: 1.7
- HIV+ / HBV+: 14.2

Pre-Treatment Evaluation
History and Physical Examination

- Risk factors for viral hepatitis
- Risk factors for HIV co-infection
- Duration of infection
- Alcohol history
- Presence of comorbid diseases
- Family history of liver cancer

- Complete physical examination
  - Hepatomegaly
  - Splenomegaly
  - Jaundice
  - Distended abdomen
  - Spider angiomata

Pre-Treatment Blood Tests

- Serial testing of ALT and HBV DNA level for 6 months
- CBC, liver enzymes, prothrombin time/INR
- Urinalysis
- HBeAg and anti-HBe
- HBV genotype including resistance testing and basal core promoter mutation
- HIV Serology, CD4 Count, HIV Viral load, Resistance testing, HLA-B*5701 Testing, Tropism Testing,

- Testing for other viruses:
  - anti-hepatitis A virus Ig G (vaccinate as needed)
  - anti-HCV Ab
  - anti-HDV Ab
  - anti-HEV Ab (particularly in acute hepatitis)
  - anti-HIV Ab
- Testing for other liver diseases in patients with abnormal liver tests:
  - ANA, ASMA
  - Fe/TIBC/ferritin

Assessing Disease Severity

• Assess the severity of liver disease:
  – FIB-4, APRI
  – Transient elastography
  – MR elastography

• Screening for liver cancer
  – Ultrasound every-6-months
  – AFP every-6-months
  – MRI in cirrhotics
Non-Invasive Formulas to Assess Severity of Fibrosis

**APRI**

\[
\text{APRI} = \frac{\text{AST Level (U/L)}}{\text{AST (Upper Limit of Normal) (U/L)}} \times \frac{\text{Platelet Count (10^9/L)}}{100}
\]

**FIB-4**

\[
\text{FIB-4} = \frac{(\text{Age (years)} \times \text{AST Level (U/L)})}{\text{Platelet Count (10^9/L)}} \times \sqrt{\text{ALT (U/L)}}
\]
Screening and Management
**Screening for HIV or HBV**

- HBV (or HIV) patients should be screened for coinfection during their initial patient evaluation\(^1\)\(^-\)\(^3\)
- The USPSTF recommends screening for HBV infection in persons at high risk\(^*\) for infection\(^5\)\(^6\)

**Treatment**

- HIV/HBV coinfected patients are indicated for therapy\(^4\)\(^,\)\(^5\)\(^,\)\(^7\)
- Therapy should have activity against both HBV and HIV\(^3\)\(^,\)\(^4\)\(^,\)\(^5\)
- Conduct resistance testing to guide ARV selection\(^3\)

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* high risk for infection includes important risk groups having a CHB prevalence of ≥ 2%, including HIV-positive patients
\(^†\) resistance to LAM and FTC is high; \(^‡\)When used in HBV/HIV-coinfected patients, ETV must be used in addition to a fully suppressive ARV regimen due to risk of resistance selection

\(^1\) Grade B recommendation

ADV, adefovir; ETV, entecavir; IFN, interferon; FTC, emtricitabine; LAM, lamivudine; LdT, Tebivudine; PegIFN, pegylated interferon; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; USPSTF, U.S. Preventive Services Task Force

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2. Martin P, et al. Clin Gastroenterol Hepatol 2015; Published online July 15, 2015:
Guideline
Recommendations
Treatment Recommendations for HIV/HBV Coinfection

DHHS and IAS preferred regimens include a TDF- (or TAF-) containing regimen

<table>
<thead>
<tr>
<th>Recommended therapy</th>
<th>DHHS</th>
<th>IAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF (with FTC or 3TC) or TAF/FTC as part of a fully suppressive ART regimen*</td>
<td>ART regimen containing TDF or TAF plus 3TC or FTC with a third ARV</td>
<td></td>
</tr>
</tbody>
</table>

*If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is ETV in addition to a fully suppressive ARV regimen

Concurrent HIV and HBV therapy

<table>
<thead>
<tr>
<th>AASLD</th>
<th>EASL</th>
<th>APASL</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAART should include: TDF + LAM or FTC</td>
<td>TAF- or TDF-based ART regimen</td>
<td>TDF + LAM or FTC + 3rd agent</td>
<td>TDF + LAM or FTC + EFV</td>
</tr>
</tbody>
</table>

Treatment Recommendations for HIV/HBV Coinfection

Consensus among American, European, and Asian-Pacific Guidelines: Strong rationale for dual anti-HBV and anti-HIV therapy

Lok ASF et al.  AASLD Practice Guideline Update. *Hepatology*. 2009
Risk of Liver Cancer
Risk of Liver Cancer

- Five to six-fold risk increase in HCC incidence among HIV-infected individuals compared with the general population and this increased risk has persisted with ART.
- HCC among individuals with HIV infection has been associated with lower CD4 T-cell counts, and high HBV DNA.
- Increased risk of HCC in coinfection in the era of TDF containing HBV active ART suggests that other factors are also important.
- HBV monoinfection- HBV DNA suppression with NRTI has been demonstrated to lower, but not eliminate, the risk of HCC.
Risk of Liver Cancer

• HIV is not sufficient to cause HCC in itself, and the exact role of HIV in promoting HCC is not well understood. A significant component of the increased risk of HCC is attributable to the increased prevalence of viral hepatitis among HIV-infected populations.

• Main predisposing factor for the development of HCC - presence of **cirrhosis**: Other cofactors that may drive HCC among HIV-infected individuals include a **higher prevalence of other known risk factors, including alcohol, and nonalcoholic steatohepatitis**

• certain mutations in the HBV viral genome are associated with a significantly increased risk of progression to HCC in individuals with HBV monoinfection (Genotypes B, C, Deletions in the pre-S region of the HBV genome)

Singh et al. AIDS 2017, 31:2035–2052
Cohort study used data from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) study, which was conducted between 1996 and 2015. NA-ACCORD pooled individual-level data from 22 HIV clinical and interval cohorts of PWH in the US and Canada. PWH aged 18 years or older with available CD4 cell counts and HIV RNA data were enrolled.

MAIN OUTCOMES AND MEASURES: HCC diagnoses were identified on the basis of review of medical records or cancer registry linkage.

109 283 PWH with 723 441 person-years of follow-up, the median (interquartile range) age at baseline was 43 (36-51) years, 93 017 (85.1%) were male, 44 752 (40.9%) were White, 44 322 (40.6%) were Black, 21 343 (19.5%) had HCV coinfection, 6348 (5.8%) had HBV coinfection, and 2082 (1.9%) had triple infection; 451 individuals received a diagnosis of HCC by 2015.

Age Distribution and Age of Hepatocellular Carcinoma (HCC) Onset by Viral Hepatitis Coinfection Groups

Viral hepatitis coinfection
- HIV and HCV positive (n=21,297)
- HIV, HBV and HCV positive (n=2,081)
- HIV and HBV positive (n=6,330)
- HIV positive, HBV and HCV negative (n=76,506)

Age at HCC
- Mean
- Median

JAMA Network Open. 2021;4(2):e2037512
HCC rates among PWH increased significantly over time from 1996 to 2015. PWH coinfected with viral hepatitis, those with higher HIV RNA levels or lower CD4 cell counts, and those who inject drugs had higher HCC risk.
AASLD Guidelines: HCC Screening in HBV

- HBV carriers at high risk for HCC, include:
  - HBsAg positive patients with cirrhosis
  - Asian or Black men over 40 years and Asian women over 50 years of age
  - Family history of HCC- first degree
  - HDV infection
  - Any carrier over 40 years with persistent or intermittent ALT elevation and/or high HBV DNA level >2,000 IU/mL

- Screening is with ultrasound examination every 6 months.

• HBV carriers at high risk for HCC, include:
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  - Family history of HCC in a first degree relative
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  - Any carrier over 40 years with persistent or intermittent ALT elevation and/or high HBV DNA level >2,000 IU/mL

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New York State
HBV Clinical Capacity
Building Resources
There are many HBV training opportunities and resources, most offering CMEs:

- CME training (live/webinar) on HBV care and treatment
- HBV evaluation and linkage to care guidance and technical assistance
- HBV clinical preceptorships

[www.hepfree.nyc](http://www.hepfree.nyc)

To learn more contact: [Hep@health.nyc.gov](mailto:Hep@health.nyc.gov)

Or contact the NYC Health Department Warm line: 917-890-0834
HBV Care Resources in NYC

• Check Hep B Patient Navigation Program
  – Provides free or low cost Hep B Patient Navigation services at eight organizations in NYC. Patient Navigators assist patients with complete testing, linkage to care, support through a full medical evaluation and treatment if recommended. [https://hepfree.nyc/check-hep-b-patient-navigation-program/](https://hepfree.nyc/check-hep-b-patient-navigation-program/)

• Linkage to Care Affordable Care Support
  – Health Department HBV testing and care services listing
    • [www.nyc.gov/health/hepb](http://www.nyc.gov/health/hepb)
    • NYC Health Department Health Map
  – Health Care Access Specialist
    • 917-890-0834
    • Hep@health.nyc.gov
**HBV Care Resources in NYC**

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- **Linkage to Affordable Care Support**
  - Health Department HBV testing and care services listing: [www.nyc.gov/health/hepb](http://www.nyc.gov/health/hepb)
  - Health Care Access Specialist [Hep@health.nyc.gov](mailto:Hep@health.nyc.gov)

- **Order HBV Patient Education Materials**: [Hep@health.nyc.gov](mailto:Hep@health.nyc.gov)


- **National Task Force on Hepatitis B** Focus on API Americans: [www.hepbtaskforce.org](http://www.hepbtaskforce.org)
For CMEs or educational opportunities, contact:

Meg Chappell, MPH
Program Manager
Empire Liver Foundation
megchappell@empireliverfoundation.org
www.empireliverfoundation.org

For questions about resources, contact:

Marie P. Bresnahan, MPH
Director, Training, Policy, and Administration
Viral Hepatitis Program
Bureau of Communicable Disease
mbresnahan@health.nyc.gov
www.hepfree.nyc
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HEP FREE NYC

@LiverEmpire  
Empire Liver Foundation (ELF)

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To stay up-to-date on viral hepatitis opportunities and events around New York City

Subscribe to the Hep Free NYC Mailing List:
Upcoming Webinars

Perinatal Hepatitis C with Dr. Kushner
   April 13, 2021 @ 4PM

Perinatal Hepatitis B with Dr. Kushner
   May 5, 2021 @ 4PM

Hepatitis C Clinical Training Series (4 weeks)
   Thursdays beginning April 29 @ 4:30PM

Hepatitis B Clinical Training Series (3 weeks)
   Thursdays beginning June 3 @ 4:30PM

To register or for more information, contact megchappell@empireliverfoundation.org