Prevalence of HBV: Global Estimates

350 million With Chronic HBV

<table>
<thead>
<tr>
<th>Country</th>
<th>HBsAg Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taiwan</td>
<td>10-13.8</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>5.7-10</td>
</tr>
<tr>
<td>China</td>
<td>5.3-12</td>
</tr>
<tr>
<td>Africa</td>
<td>5-19</td>
</tr>
<tr>
<td>Philippines</td>
<td>5-16</td>
</tr>
<tr>
<td>Thailand</td>
<td>4.6-8</td>
</tr>
<tr>
<td>Japan</td>
<td>4.4-13</td>
</tr>
<tr>
<td>Indonesia</td>
<td>4.0</td>
</tr>
<tr>
<td>South Korea</td>
<td>2.6-5.1</td>
</tr>
<tr>
<td>India</td>
<td>2.4-4.7</td>
</tr>
<tr>
<td>Russia</td>
<td>1.4-8</td>
</tr>
<tr>
<td>United States</td>
<td>0.2-0.5</td>
</tr>
</tbody>
</table>

New HBV Infections by Year:
United States (1966-2006)

HBV and Hepatocellular cancer (HCC)

- Globally, most common underlying cause of HCC
- In Asia, up to 40% of HCC in HBV in noncirrhotics
- Western countries show significantly less risk in HBV carriers
- Annual incidence: 0.2% to 2.5%


ACG 2016 Midwest Hepatitis School
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Hepatitis B: Natural History

- If it is not treated, in 1/3 of patients, hepatitis B can cause liver damage leading to cirrhosis and liver cancer\(^1\)

- Hepatitis B is responsible for 80% of primary liver cancer globally, which is almost always fatal\(^2\)
  - Liver cancer is the 2\(^{nd}\) highest cause of death by cancer \(^3\)
  - Without appropriate treatment or monitoring, 1 in 4 persons with chronic hepatitis B will die of liver cancer or liver disease

---

\(^1\) WHO. Available at: www.who.int/csr/disease/hepatitis/en/;
Natural History of Chronic HBV Infection

Childhood

>95% → Immune Tolerance

Adulthood

<5% → HBeAg+ CHB

HBeAg- CHB → Inactive carrier

<15-30% of HCC associated with HBV occurs in the absence of cirrhosis or advanced fibrosis

HCC And or cirrhosis


HBV DNA vs. Liver Cirrhosis: REVEAL data

No of patients =3,482*

Cumulative rate of Liver Cirrhosis

Baseline HBV DNA

≥10^5 copies/mL

10^4<10^5

10^3<10^4

300<10^3

<300

Years

* HBeAg negative n=2360

**HBV DNA vs. HCC: REVEAL Data**

<table>
<thead>
<tr>
<th>HBV DNA Level</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10^9 copies/mL</td>
<td>6.6</td>
</tr>
<tr>
<td>10^4–10^6</td>
<td>6.1</td>
</tr>
<tr>
<td>300–10^4</td>
<td>2.3</td>
</tr>
<tr>
<td>&lt;300</td>
<td>1.1</td>
</tr>
</tbody>
</table>

*HBeAg negative n=3086

**Aiming for True Inactive Carrier Status**

1. **Milestone 1:** Start of decline of HBV DNA<br>2. **Milestone 2:** HBeAg/anti-HBe seroconversion<br>3. **Milestone 3:** HBV DNA decreased to undetectable<br>4. **Milestone 4:** Clearance of HBsAg<br>5. **Milestone 5:** Clearance of cccDNA

- Low HBV DNA (<2000 IU/mL) for reduced progression risk

This is where we would like our patients to be.

**Functional cure**

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Goals of therapy for Hepatitis B

Liver histology Improves
Serum HBV DNA declines

Prevention of Death, Cirrhosis, and HCC

Seroconversion (loss of HBeAg, production of anti-Hbe, loss of HBsAg)
ALT normalization

US FDA dates of Approved Therapies for CHB

<table>
<thead>
<tr>
<th>Nucleosides/Nucleotides</th>
<th>Approved Date</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir*</td>
<td>2008</td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>2006</td>
<td>Idenix / Novartis</td>
</tr>
<tr>
<td>Entecavir*</td>
<td>2005</td>
<td>Bristol-Myers Squibb</td>
</tr>
<tr>
<td>Adefovir dipivoxil</td>
<td>2002</td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>1998</td>
<td>GlaxoSmithKline</td>
</tr>
</tbody>
</table>

| Interferons                     |               |                           |
| Peginterferon alfa-2a*          | 2005          | Roche Laboratories         |
| Interferon alfa-2b, recombinant | 1992          | Schering / Merck           |

Preferred therapies – AASLD Guidelines
Candidates for HBV Treatment

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA threshold (IU/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBeAg positive</td>
<td>20,000</td>
<td>2000</td>
<td>20,000</td>
<td>20,000</td>
</tr>
<tr>
<td>HBeAg negative</td>
<td>2000</td>
<td>2000</td>
<td>2000</td>
<td>2000</td>
</tr>
<tr>
<td>ALT:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal range</td>
<td>-</td>
<td>-</td>
<td>(M: 30 U/L; F: 19 U/L)</td>
<td>2X ULN (M: 30 U/L; F: 19 U/L)</td>
</tr>
<tr>
<td>When to treat:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>key factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy</td>
<td>Consider in certain groups</td>
<td>Consider in certain groups</td>
<td>Consider in certain groups</td>
<td>Consider in certain groups</td>
</tr>
</tbody>
</table>

Other Caveats From Recent AASLD Guideline Update

- The decision to treat persons with ALT above the ULNs, but <2 ULN, requires consideration of severity of liver disease (defined by biopsy or noninvasive testing).
- Therapy is recommended for persons with immune-active CHB and cirrhosis if HBV DNA >2,000 IU/mL, regardless of ALT level.
- The AASLD suggests antiviral therapy in the select group of adults >40 years of age with normal ALT and elevated HBV DNA (1,000,000 IU/mL) and liver biopsy showing significant necroinflammation or fibrosis.

### Treatment Guidelines: Recommendations for First-Line Therapy in Patients Without Cirrhosis

**HBeAg Positive or Negative Chronic HBV**

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Alternative</th>
<th>Not Preferred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir DF</td>
<td>Adefovir</td>
<td>Lamivudine</td>
</tr>
<tr>
<td>Entecavir</td>
<td>Telbivudine*</td>
<td></td>
</tr>
<tr>
<td>Peg-IFN alpha-2a</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*HBV DNA must be undetectable at 24 weeks to continue (Keeffe). AASLD guidelines: lamivudine and telbivudine not preferred due to relatively high rate of resistance. Adefovir not preferred due to weak antiviral activity and relatively high rate of resistance in HBeAg-negative studies.


### Treatment Guidelines: Recommendations for Patients With Cirrhosis

**Compensated Cirrhosis**

- **Preferred:**
  - Tenofovir DF
  - Entecavir
- **Potential:**
  - Peg-IFN alpha-2a*
- **Not Preferred:**
  - Lamivudine
  - Telbivudine

**Decompensated Cirrhosis**

- **Preferred:**
  - Tenofovir DF
  - Entecavir
- **Not Preferred:**

*Note: therapies are approved for monotherapy only.
*Early cirrhosis only.
†Contraindicated.

Decrease in Serum HBV DNA after 1 Year of Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Log10 Decrease in HBV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAM</td>
<td>-5.5</td>
</tr>
<tr>
<td>ADV</td>
<td>-3.5</td>
</tr>
<tr>
<td>ETV</td>
<td>-6.9</td>
</tr>
<tr>
<td>TBV</td>
<td>-6.6</td>
</tr>
<tr>
<td>TDF</td>
<td>-6.2</td>
</tr>
<tr>
<td>PEG-IFN</td>
<td>-3.0</td>
</tr>
</tbody>
</table>

Not head-to-head comparison, results from various trials combined

HBeAg Seroconversion after 1-5 Years of Treatment

At 1 Year

<table>
<thead>
<tr>
<th>Drug</th>
<th>HBeAg Seroconversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg</td>
<td>32</td>
</tr>
<tr>
<td>LMV</td>
<td>16-21</td>
</tr>
<tr>
<td>ADV</td>
<td>12-18</td>
</tr>
<tr>
<td>ETV</td>
<td>21</td>
</tr>
<tr>
<td>TBV</td>
<td>22</td>
</tr>
<tr>
<td>TDF</td>
<td>21</td>
</tr>
</tbody>
</table>

> 1 Year

<table>
<thead>
<tr>
<th>Drug</th>
<th>HBeAg Seroconversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg</td>
<td>~35</td>
</tr>
<tr>
<td>LMV</td>
<td>~50</td>
</tr>
<tr>
<td>ADV</td>
<td>48</td>
</tr>
<tr>
<td>ETV</td>
<td>41</td>
</tr>
<tr>
<td>TBV</td>
<td>42</td>
</tr>
<tr>
<td>TDF</td>
<td>40</td>
</tr>
</tbody>
</table>

Peg = peginterferon
LMV = lamivudine
ADV = adefovir
ETV = entecavir
TBV = telbivudine
TDF = tenofovir

@ 6 months off Rx
^ 3 years off Rx
# 5 years on Rx
* 4 years on Rx
HBsAg Loss after 2-5 Years of Treatment

Peg = peginterferon
LMV = lamivudine
ADV = adefovir
ETV = entecavir
TBV = telbivudine
TDF = tenofovir

^ 3 years off Rx
# 4-5 years on Rx
* 2 years on Rx

Reversal of Fibrosis and Cirrhosis
Tenoforv Phase III Trial: Biopsies at Year 0, 1 & 5

• 348/641 (54%) had liver biopsy at baseline and Year 5
• 71/96 (74%) with cirrhosis (Ishak Score ≥5) at baseline no longer had cirrhosis at Year 5

Marcellin, P, Lancet 2013; 381: 468
Antiviral Therapy Prevents Disease Progression
Bridging fibrosis or cirrhosis, HBeAg+ / HBV DNA >140,000 IU/mL

% with disease progression

Increase CTP score, liver failure or HCC

Time to disease progression (months)

Placebo (n=215) ITT population
Lamivudine (n=436) p=0.001

Liaw YF, NEJM 2004; 351:1521

Efficacy and Limitations of Currently Available HBV Therapies

• Potent viral suppression
• Reverse hepatic fibrosis / cirrhosis
• Prevent progression to liver failure
BUT
• Low rate of HBsAg loss
• Decrease but not eliminate incidence of HCC
• Long duration / lifelong treatment required to maintain benefit
  • High costs, risks of drug resistance and side effects
Patients with HBV DNA ≥ 400 copies/mL at Week 72 could add FTC to TDF; * Cumulative probabilities of resistance taken; † Naïve HBeAg (+); ‡ Naïve HBeAg(-); N/A not available.


Resistance Rates Through 6 Years Among Nucleos(t)ide-Naïve Patients

Study ETV-901: 5-Year Durable Efficacy of Entecavir in HBeAg-Positive Patients

- Long-term observational roll-over study
  - Previously treatment-naïve patients (n=146)
- Long-term entecavir
  - 94% undetectable through 5 years
  - Maintained ALT normalization
  - Entecavir resistance in 1 patient (1%)
  - Experienced virologic breakthrough at year 3

Outcomes

Studies 102/103: Virologic Suppression With Tenofovir at Year 8

<table>
<thead>
<tr>
<th></th>
<th>HBeAg-</th>
<th>HBeAg+</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA &lt;29 IU/mL (ITT)* %</td>
<td>74</td>
<td>58</td>
</tr>
<tr>
<td>HBV DNA &lt;29 IU/mL (Observed), %</td>
<td>99.6</td>
<td>97</td>
</tr>
<tr>
<td>HBeAg loss / seroconversion†, %</td>
<td>NA</td>
<td>47/31</td>
</tr>
<tr>
<td>HBsAg loss / seroconversion (KM%)‡</td>
<td>1.1/0.7</td>
<td>12.9/10.3</td>
</tr>
</tbody>
</table>

*Missing = failure; add FTC = failure<br>*Missing = excluded; add FTC = included<br>‡ KM-ITT<br>NA, not applicable

Marcellin, AASLD, 2014, Oral #229

HCC Risk in Caucasian, Chronic HBV Patients Treated With Entecavir or Tenofovir DF

- Multi-country cohort (Greece, Italy, Turkey, Spain, The Netherlands) (n=1231)
  - Chronic HBV with no co-infection, liver transplantation, or HCC
  - Initiated either entecavir (43%) or tenofovir DF (55%)
- HCC 5-year incidence
  - 4.2% at median of 17 months
  - 13.5 new HCC cases/1000 person-years
- Strongest HCC risk factors
  - Decompensated liver disease (HR: 2.78; P=0.015), lower platelet count (HR: 0.97; P=0.002), older age (HR: 1.05; P=0.12)
- Asian-based HCC risk scores may not be applicable to Caucasians with chronic HBV

NIDDKD Cohort: HBsAg Loss by Mode of HBeAg Clearance

- Treatment-induced HBeAg clearance (n=51)
  - Interferon related: 86%
- Cumulative incidence of HBeAg loss per year (P=0.02)
  - Spontaneous: 1.6%
  - Nucleoside analog induced: 4.4%
  - Interferon induced: 6.3%
- Most significant predictors of HBsAg loss
  - Mode of HBeAg loss
  - Race

Probability of HBsAg Loss by Mode of HBeAg Clearance


HBsAg Loss in HBeAg-Positive and HBeAg-Negative Patients

When can treatment be stopped?

PEG IFN → defined duration, 12 months for both HBeAg+ and HBeAg- patients

Nucleos(t)ide analogues → until treatment endpoint

- HBeAg+ patients → HBeAg seroconversion + ≥12 mos consolidation Rx, ~50% after 5 yr Rx
  
  An alternative approach is to treat until HBsAg loss.

- HBeAg- patients → Indefinite therapy
  
  HBsAg loss ~5% after 5 yr Rx

- Cirrhotics → life-long Rx


New Polymerase inhibitor Coming

- Tenofovir alafenamide (TAF)
  - New tenofovir (TFV) produg; greater plasma stability than TDF<sup>1-3</sup>
  - Enhances delivery of active drug (TFV-DP) to hepatocytes<sup>1-3</sup>
  - Reduces circulating levels of TFV relative to TDF<sup>4,5</sup>
  - Improved bone and renal safety demonstrated in HIV patients<sup>5,6</sup>

- Study aim
  - To evaluate efficacy and safety of TAF compared with TDF in HBeAg+ patients with chronic hepatitis B
**Tenofovir alafenamide versus tenofovir disoproxil**

- Double-blind, active-controlled, Phase 3 study
- Key inclusion criteria:
  - HBeAg-positive at screening
  - HBV DNA ≥20,000 IU/mL; ALT >60 U/L (males), >38 U/L (females)
- 2:1 randomization
  - Stratified by HBV DNA level and treatment status (naive vs experienced)

---

**Chan et al EASL 2016**

**Similar efficacy, better safety profile**

- Improved renal safety profile
- Improved bone turnover parameters
Cirrhosis Reversal Following Lamivudine Rx in HBV

Types of Virological Response

HBV DNA (Log10 IU/ml)

On Treatment

Relapse

Sustained Response

On Continuous Treatment

Primary non-response

Breakthrough

Breakthrough

Maintained Response
Not head to head trials
Different patient populations and trial designs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>24</td>
<td>43</td>
<td>65</td>
<td>82</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>Adefovir</td>
<td>5</td>
<td>42</td>
<td>70</td>
<td>63</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Entecavir</td>
<td>0.4</td>
<td>0.4</td>
<td>1.0</td>
<td>3.4</td>
<td>9.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>2.9</td>
<td>11.6</td>
<td>18.1</td>
<td>16.5</td>
<td>4.2</td>
<td>0</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>


Summary: Guidelines for Management of Antiviral-Resistant HBV

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Rescue Therapy</th>
</tr>
</thead>
</table>
| Lamivudine | Add tenofovir DF  
Stop lamivudine, switch to tenofovir DF |
| Adefovir   | Add lamivudine  
Stop adefovir, switch to:  
Emtricitabine/tenofovir DF  
Switch to or add entecavir (if no prior lamivudine resistance) |
| Entecavir  | Switch to tenofovir DF or add tenofovir DF |
| Telbivudine| Add tenofovir DF  
Stop telbivudine, switch to tenofovir DF |
| Multi Drug | Tenofovir DF + entecavir |

Indications for HBV vaccination

- HBIG and HB vaccine to infants of HBsAg+ mothers
- Routine vaccination of infants and adolescents
- Catch-up vaccination of children
- Vaccination of adults at risk of infection

**HBV DNA Level and Perinatal Transmission of HBV**

No cases of transmission from mothers with HBV DNA <3 log\textsubscript{10} copies/mL. One case of escape mutation identified.

Treatment during pregnancy

AASLD suggests antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in HBsAg-positive pregnant women with an HBV DNA level >200,000 IU/mL.

<table>
<thead>
<tr>
<th>HBsAg(+) pregnant women</th>
<th>Lamivudine (100 mg/day) from 32 ± 2 weeks of gestation to 4 weeks postpartum (n = 56)</th>
<th>Placebo (n = 59)</th>
<th>All infants received</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA &gt; 1000 mEq/mL</td>
<td></td>
<td></td>
<td>HBV vaccine (10 g/0.5 mL)</td>
</tr>
<tr>
<td>(n = 114)</td>
<td></td>
<td></td>
<td>HBIG (200 IU, single dose)</td>
</tr>
</tbody>
</table>

Primary endpoint HBsAg + infant at 1 yr
Secondary endpoint HBsAb+, HBV DNA+


Xu et al: Improved outcomes for the infants

<table>
<thead>
<tr>
<th>Infant Status at 52 weeks</th>
<th>LAM (n = 56)</th>
<th>Placebo (n = 59)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg(+), %</td>
<td>18</td>
<td>39</td>
<td>.014</td>
</tr>
<tr>
<td>HBV DNA(+), %</td>
<td>20</td>
<td>46</td>
<td>.003</td>
</tr>
</tbody>
</table>

HBsAb positive 84% vs. 61% (p=0.008)

- Lamivudine, telbivudine, and tenofovir may be used, started at 28-32 weeks of gestation
- Antiviral therapy was discontinued at birth to 3 months postpartum, monitor for flares
- Breastfeeding is not contraindicated.

Treatment of HBV: Special Cases

- **Prophylactic treatment during chemotherapy to prevent reactivation** (Rx from 1 wk before to 3-12 mo after)
  - % with hepatitis: 53% untreated vs. 14% lamivudine-treated

- **Treatment of women during the third trimester of pregnancy to reduce rate of vertical transmission**
  - Studies limited; use in women with HBV DNA $>10^8$ c/mL

- **HBV/HIV coinfection**
  - If HAART needed, then tenofovir + emtricitabine or lamivudine

- **Prophylactic treatment after liver transplantation to prevent reinfection**


HBV Reactivation Following Rituximab-Containing Chemotherapy

- **Single-center cohort with a variety of hematologic diagnoses** (n=62) (2011-2013)
  - HBsAg negative, anti-HBc positive
  - HBV DNA $<$10 IU/mL
  - No concomitant liver disease or prior HBV treatment
  - Reactivation: HBV DNA $>10$ IU/mL regardless of HBsAg status
  - Follow-up: 36.6 months

- **High rate of reactivation**
  - Majority occurred within the first 6 months (86.7%) 
  - Presence of low anti-HBs levels was not protective against HBV reactivation

Hepatitis B reactivation recommendations
High-Risk Patients (Anticipated Incidence of HBV Reactivation, >10% of Cases)

- Tenofovir/Entecavir preferred agents
- Continue antiviral therapy for at least 6 months after discontinuation of immunosuppressive therapy (at least 12 months for B-cell–depleting agents).
  - Hepatitis B surface antigen (HBsAg)-positive/anti-hepatitis B core antibody (HBc)–positive patients treated with B-cell–depleting agents (eg, rituximab, ofatumumab)
  - HBsAg-positive/anti-HBc–positive patients treated with anthracycline derivatives (eg, doxorubicin, epirubicin)
  - HBsAg-positive/anti-HBc–positive patients treated with moderate-dose (10-20 mg prednisone daily or equivalent) or high-dose (>20 mg prednisone daily or equivalent) corticosteroids daily for ≥4 weeks.


Hepatitis B reactivation recommendations
Moderate-Risk Patients (HBV Reactivation, 1%-10% of Cases)

- Tenofovir/Entecavir preferred, continue treatment for 6 months after discontinuation of immunosuppressive therapy
- HBsAg-positive/anti-HBc–positive or HBsAg-negative/anti-HBc–positive patients treated with tumor necrosis factor alpha inhibitors (eg, etanercept, adalimumab, certolizumab, infliximab)
- HBsAg-positive/anti-HBc–positive or HBsAg-negative/anti-HBc–positive patients treated with other cytokine or integrin inhibitors (eg, abatacept, ustekinumab, natalizumab, vedolizumab)
- HBsAg-positive/anti-HBc–positive or HBsAg-negative/anti-HBc–positive patients treated with tyrosine kinase inhibitors (eg, imatinib, nilotinib)
- HBsAg-positive/anti-HBc–positive patients treated with low-dose (<10 mg prednisone daily or equivalent) corticosteroids for ≥4 weeks
- HBsAg-negative/anti-HBc–positive patients treated with moderate-dose (10-20 mg prednisone daily or equivalent) or high-dose (>20 mg prednisone daily or equivalent) corticosteroids daily for ≥4 weeks
- HBsAg-negative/anti-HBc–positive patients treated with anthracycline derivatives (eg, doxorubicin, epirubicin).
How do we screen for HCC in HBV

- No studies define unequivocally the best modality for diagnosing HCC
- Ultrasonography (US) every 6 months with alpha-fetoprotein (AFP) every six months is current standard of care for screening high risk patients
  - US has technical limitations (operator dependence, reduced efficacy in those with elevated BMI)
  - US if subject has normal BMI
- AFP alone is not sufficient unless imaging modalities are not available
- Our practice at IU: MRI every 9 months or Dual Phase Spiral CT, or US every 6 months if normal BMI
  - MRI or US preferred due to radiation risk with CT scan

AASLD Guidelines: HBV

- Surveillance recommended in at-risk groups
  - Specific hepatitis B carriers
    - Asian males >40 years
    - Asian females >50 years
    - Africans >20 years
    - All HBV cirrhotic pts
    - Family history of hepatoma
- Patients should be screened at 6-month intervals
  - US and AFP level
**Other Clinical Pearls**

- Avoid entecavir use in HBV/HIV
  - leads to HIV resistance
  - Check HIV serology prior to initiating entecavir
- Telbivudine /tenofovir are pregnancy category B
  - Useful in young females trying to conceive
  - Acute HBV in pregnancy
  - Low rate of resistance if HBV undetected by week 24 but must monitor for resistance

---

**Indications for treatment of chronic hepatitis B**

**Who Should be Treated?**

- Chronic HBV infection: HBsAg+ >6 months
- Evidence of virus replication: serum HBV DNA >10^{4-5} copies/mL (2000-20,000 IU/mL)
- Evidence of liver damage: elevated ALT and/or chronic hepatitis on biopsy
Summary

Prevention
- Avoid unnecessary treatment
- Initiate treatment with potent antiviral that has low rate of drug resistance (tenovir or entecavir) or with combination therapy
- Switch to alternative therapy in patients with primary non-response

Monitoring
- Test for serum HBV DNA (PCR assay) every 3-6 months during treatment
- Check for medication compliance in patients with virologic breakthrough
- Confirm antiviral resistance with genotype testing

Summary of Guidelines

Treatment of Hepatitis B

When to start therapy
- Elevated HBV DNA [≥20,000 IU/mL for HBeAg(+) and 2,000 IU/mL for HBeAg(-)] plus elevated ALT, and/or significant disease on liver biopsy

When to stop or alter therapy
- HBeAg(+): HBeAg seroconversion and (-) HBV DNA
- HBeAg(-): ?long-term therapy
- Inadequate VR (≥2,000 IU/mL) at week 24
- Development of antiviral drug resistance