Hepatitis B and C: Clinical Tools for Efficient Management in Primary Care

Primary Care Update: 2012

Rena K. Fox, M.D.
Associate Professor of Clinical Medicine and Medical Editor, National VA Hepatitis C Website

HCV Outcomes in Next 20 Years

↑ 106% Decompensated liver disease
↑ 81% HCC
↑ 180% Liver related death


Deaths Due to Hepatitis C Now Exceed Deaths Due to HIV in the U.S.


Hepatitis C Infection
1 in 33 Baby Boomers

Natural History and potential clinical outcomes in HCV

- **Acute HCV infection**
  - 15% Spontaneously resolve
    - No chronic infection
    - Ab+, RNA -
  - 85% Chronic HCV
    - Variable natural history
    - Ab+, RNA +

- **Variable degrees of liver disease**
  - 20% Cirrhosis
  - Asymptomatic fibrosis
    - Stable or progressive

- **Potential determinants of disease progression**
  - Alcohol
  - HIV, Immunosuppression
  - HCV RNA – viral load
  - HCV Genotype
  - Mode of acquisition
  - Ethnicity
  - Duration
  - ALT elevation

Interpretation of HCV Diagnostic Tests

<table>
<thead>
<tr>
<th>HCV Ab</th>
<th>HCV RNA</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Acute or chronic HCV</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Spontaneous resolution of HCV; successful treatment of HCV; Acute phase with low level viremia</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Early acute HCV; Chronic HCV with immunocompromised state and false negative Ab; false positive RNA</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>No HCV infection</td>
</tr>
</tbody>
</table>

Initial Evaluation of Patient with HCV

- **History** – risk factors, family, social, sexual, occupational, alcohol and drug history, estimate duration of infection
- **Physical** – Signs of liver disease, splenomegaly
- **Initial laboratories**
  - RNA, Genotype, HIV Ab, HBsAg, HBsAb, HBCAb, HAVAb
  - CBC, platelet, INR, Albumin, AST, ALT, Alkphos, Bili, TSH, Fasting glucose, Creatinine, Lipids
- **Consider biopsy** if considering treatment or patient desires prognostic information
- **Consider ultrasound** if biopsy not planned to look for any evidence of cirrhosis or portal hypertension
- **Counseling** – BMI, alcohol, sexual, household transmission
- **Vaccination** for HBV and HAV if not immune
- **Refer** to GI-Liver if motivated for treatment or decompensated or co-infected HIV or HBV
Understanding HCV RNA Testing: Do Not Routinely Follow the HCV Viral Load!!!

- HCV RNA mandatory to make Chronic HCV diagnosis
- But, Quantitative RNA (Viral Load)
  - Does not correlate with degree of fibrosis
  - Does not predict progression of disease
  - Does not change significantly over time
- Necessary for treatment – before, during, after
  - Pre-treatment viral load predictive of success
  - Change in RNA reflects response
- But if not on HCV treatment, no role for viral load
  - Will not change management
  - Confuses patients about state of their HCV disease

The Non-Significance of ALT in Hepatitis C

- 1/3 have normal ALT
- ¼ have ALT >2x upper limit normal
- Remainder are slightly elevated
- Poor correlation between level and histology
- Does not predict response to treatment
- ALT normalization does not correlate with histological changes from therapy

Antiviral Treatment of HCV

- Aim of treatment
  - Slow or halt progression to cirrhosis
  - Reduce progression to decompensation
  - Reduce risk of liver related deaths
  - Reduce risk of hepatocellular carcinoma

- 1 Regimen only since 2001
  - Pegylated interferon and ribavirin
  - Genotype 1 = 48 weeks, Genotype 2,3 = 24 weeks

New Drugs for HCV – May 2011

Protease inhibitors - Telaprevir, Boceprevir

**Boceprevir**
- FDA approved May 13, 2011
- [http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm255390.htm](http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm255390.htm)

**Telaprevir**
- FDA approved May 23, 2011
- [http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/ucm206328.htm](http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/ucm206328.htm)
Patterns of Response to Treatment

- Nonresponder
- Sustained responder
- Relapser

Effect of HCV Treatment on HCV RNA

- Sustained Virological Response (SVR)
  Virus is not replicating, completely suppressed
  Response persists 6 months after treatment is stopped
  Qualitative HCV RNA undetectable is definitive assay

- SVR rates - Pegylated Interferon + Ribavirin
  Genotype 1: 42-46%
  Genotype 2,3: 76-82%

- Long Term Data
  99% still remain RNA undetectable 5 yrs after treatment

SVR Associated With Improved Clinical Outcomes

- SVR
  - Durable
  - Leads to improved histology
  - Leads to clinical benefits
    - Decreases decompensation
    - Prevents de novo esophageal varices
    - Decreases risk of hepatocellular carcinoma
    - Decreases mortality

Contraindications to HCV Treatment

- Major uncontrolled depressive illness
- Pregnancy or unwilling to comply with contraception
- Autoimmune condition which may be exacerbated by interferon
- Solid organ transplant
- Severe concurrent medical condition such as uncontrolled HTN, CHF, CAD, COPD, DM
- Severe untreated thyroid disease

Ghany MG et al, Hepatology 2009:49:1335
Which Patients Should Be Treated?

Consider every patient for treatment, including:
- HIV-HCV infected patients
- Cirrhotic patients
- Normal ALT
- High HCV RNA viral load

Boceprevir and Telaprevir both approved in May 2011

Boceprevir Phase III trials
- SPRINT-2: naive Genotype 1 (GT1) patients
- RESPOND-2: nonresponder GT1 patients (partial responders and relapers)

Telaprevir Phase III trials
- ADVANCE: naive GT1 patients
- ILLUMINATE: response-guided therapy in naive GT1 patients
- REALIZE: nonresponder GT1 patients (null responders, partial responders, relapers)

Both Protease Inhibitors Improve Results for HCV Genotype 1 Infection

- SVR improved with telaprevir + PEG-IFN/RBV compared to PEG-IFN/RBV
  - Treatment naïve patients: SVR 61-69% vs 41-46%
  - Prior non-responders / relapers: SVR 51-53% vs 14%

- SVR improved with boceprevir + PEG-IFN/RBV compared to PEG-IFN/RBV
  - Treatment naïve patients: SVR 63-66% vs 38%
  - Prior partial responders / relapers: SVR 52-75% vs. 7-29%

How Will We Use Protease Inhibitors for HCV?

- Initial paradigm to be approved will be addition of DAA to pegIFN/RBV
  - Will substantially improve therapeutic possibilities for many GT1 patients

- However, challenging patient scenarios will remain, including
  - Previous null responders and other patients with adverse prognostic factors: is the improvement in SVR rate with telaprevir or boceprevir “good enough”?
  - Patients who cannot tolerate pegIFN, RBV, and/or the adverse events associated with telaprevir or boceprevir
  - Patients who cannot adhere to complex regimens for 6-12 mos; risk of resistance with suboptimal adherence
  - Others: Patients with end-stage renal disease, HCV/HIV coinfection, transplants
SVR Rates by host *IL28B* genotype

<table>
<thead>
<tr>
<th>Caucasians</th>
<th>African Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs12979860</td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>12%</td>
</tr>
<tr>
<td>CT</td>
<td>39%</td>
</tr>
<tr>
<td>TT</td>
<td>49%</td>
</tr>
<tr>
<td>rs12979860</td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>37%</td>
</tr>
<tr>
<td>CT</td>
<td>48%</td>
</tr>
<tr>
<td>TT</td>
<td>15%</td>
</tr>
</tbody>
</table>


Multivariate Analysis of Baseline Predictors of SVR (Genotype 1 HCV)

ITT analysis of patients from IDEAL study who consented to genetic testing, regardless of adherence level (n = 1604) plus 67 patients from another trial

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs12979860 CC</td>
<td>5.2 (4.1-6.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>HCV RNA level ≤ 600,000 IU/mL</td>
<td>3.1 (2.3-4.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>White vs black</td>
<td>2.8 (2.0-4.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hispanic vs black</td>
<td>2.1 (1.3-3.6)</td>
<td>.0041</td>
</tr>
<tr>
<td>METAVIR F0-F2</td>
<td>2.7 (1.8-4.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Fasting blood sugar &lt; 5.6 mmol/L</td>
<td>1.7 (1.3-2.2)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>


Epidemiology of HBV in the U.S.

1980s: 430,000 new cases of HBV infection occurred each year in the U.S.

1997: 185,000 new cases of HBV infection per year in the U.S.

Current burden of hepatitis B

- **Globally**
  - 50 million new cases per year
  - 400 million chronically infected; 75% in Asia
  - 520,000 deaths per year
- **15–40%** of those with chronic hepatitis B are expected to progress to cirrhosis, end-stage liver disease, or hepatocellular carcinoma
- **Highly linked to hepatocellular carcinoma (HCC), the fifth most common cause of cancer deaths world-wide**

MMWR 2004; 51: 1252

Burden of hepatitis B in the US

- 1.25 million chronic infected; 0.3% of adult population
- Immigration from areas endemic for hepatitis B infection, including Asia, has an impact on the US pattern of disease
- 4–5,000 deaths per year
- Current vaccination policies have markedly reduced new infections but cannot address prevalent infections

Chronic Hepatitis B in the US: Undiagnosed and Undertreated

~ 2 million people have chronic hepatitis B
400,000-600,000 diagnosed
200,000-300,000 entered into care
< 50,000 are receiving antiviral treatment

Hepatitis B Clinical Terminology

**Chronic hepatitis B**
Chronic inflammatory disease of the liver due to persistent infection from HBV; subdivide eAg(+) or (-)

**Inactive HBsAg carrier state**
Persistent HBV w/o significant ongoing inflammation

**Resolved hepatitis B**
Previous HBV without further virologic, biochemical, histological infection or disease

**Reactivation of hepatitis B**
Reappearance of active disease in person known to have inactive or resolved HBV

**HBeAg clearance; e Antigen seroconversion**
Loss of HBeAg and detection anti-HBe in person previously HBeAg (+)

Serologic Markers in HBV Infection

- **HBsAg**
  - Marker of chronic hepatitis B when found in serum > 6 mos
- **Anti-HBs**
  - Marker of immunity
- **HBeAg**
  - An index of active viral replication and high infectivity
- **Anti-HBe**
  - Appears in recovery phase or reactivation phase
- **Anti-HBc**
  - Marker of past and possibly current infection
- **Anti-HBcIgM** – marker of acute infection
HBV Genotypes: Epidemiology

- HBV classified into 8 well-documented genotypes (A-H)
  - A: North America, Western Europe, and Africa
  - B and C: Asia
  - D: Southern Europe, Africa, and India
  - E: West Africa
  - F: Central and South America and Alaska
  - G: United States, France, and Germany
  - H: Central America
- Genotype B associated with less active disease, slower progression, and lower incidence of HCC than genotype C
- Genotypes A and B respond better to IFN than genotypes C and D


Outcome of Hepatitis B Virus Infection by Age at Infection

<table>
<thead>
<tr>
<th>Age at Infection</th>
<th>Chronic Infection (%)</th>
<th>Symptomatic Infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>1-6 mos</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>7-12 mos</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>1-4 yrs</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Older Children and Adults</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Phases of Chronic HBV Infection

<table>
<thead>
<tr>
<th>Typical HBV DNA, IU/mL</th>
<th>Immune Tolerance</th>
<th>Immune Active/ HBeAg Positive CHB</th>
<th>Nonreplicative (Inactive Carrier)</th>
<th>HBeAg-Negative CHB</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 200,000 and often &gt; 10^4</td>
<td>Normal</td>
<td>Elevated or fluctuating</td>
<td>Normal</td>
<td>Elevated or fluctuating</td>
</tr>
<tr>
<td>HBeAg Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Nonreplicative (Inactive Carrier)</td>
</tr>
<tr>
<td>ALT Normal</td>
<td>elevate or fluctuating</td>
<td>Normal</td>
<td>Elevated or fluctuating</td>
<td>HBeAg-Negative CHB</td>
</tr>
<tr>
<td>Histology</td>
<td>Liver biopsy typically normal or minimal findings</td>
<td>Active inflammation on liver biopsy</td>
<td>HBsAg may become undetectable</td>
<td>Active inflammation on liver biopsy</td>
</tr>
<tr>
<td>Treatment candidate?</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>


Natural History Depends on Transmission

- Mother-to-child transmission
- Person-to-person transmission
- Clearance of HBeAg

- Immune-tolerant phase
- Immune-active phase
- Inactive carrier phase
- Cirrhosis
- Hepatocellular carcinoma

NIH Consensus Statement, 2009
A model of the natural history of chronic viral hepatitis

Factors Associated with Progression of HBV-related Liver Disease
- Older age (longer duration infection)
- HBV genotype C
- High levels HBV DNA
- Alcohol
- Coinfection with HCV, HDV or HIV
- Carcinogens (aflatoxin)
- Smoking

Dynamic Nature of Carrier State
After spontaneous HBeAg seroconversion, 67% to 80% of carriers remain in inactive carrier phase

Differentiating HBeAg-Negative Chronic Hepatitis B From Inactive Carrier State

<table>
<thead>
<tr>
<th>Status</th>
<th>HBeAg-Negative Disease</th>
<th>Inactive Carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg positive</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Anti-HBe positive</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Anti-HBc positive</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HBV DNA</td>
<td>Moderate, often fluctuating levels; mean HBV DNA &gt; 2000 IU/mL</td>
<td>Low or undetectable; mean HBV DNA &lt; 2000 IU/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>Elevated, often fluctuating levels</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Serial testing is necessary during the “inactive carrier state”
Meaning of HBeAg positivity

- HBeAg is a protein from the precore region of virus
- HBeAg spontaneously seroconverts to anti-HBe in 2 settings:
  1. Acute infection, prior to conversion of HBsAg to HBsAb
  2. Or, may occur up to decades after infection in those with chronic HBV
- Loss of HBeAg usually coincides with drop in DNA level and remission of liver disease
- Some continue to have active liver disease and high level DNA after HBeAg loss (precore mutants)

New Understanding of HBeAg-negative disease

- May represent the late phase in the natural history of chronic HBV
- More common in childhood > adult infections
- HBeAg (-) variants have mutations in core promoter and/or pre-core region of genome
- Still high level of viral replication occurs
- HBeAg (-) can still develop cirrhosis or HCC
- Responds to antiviral medications but high relapse rate after discontinuation

Hepatitis B Serologic Markers

<table>
<thead>
<tr>
<th></th>
<th>Acute hepatitis B</th>
<th>Recovery from acute hepatitis B</th>
<th>Chronic hepatitis B</th>
<th>Chronic inactive hepatitis B</th>
<th>Successful vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td></td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Anti-HBc IgM</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>HBeAg</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>HBV DNA</td>
<td>(may be only marker during window period)</td>
<td>x</td>
<td>(mod - high level)</td>
<td>x</td>
<td>(low level)</td>
</tr>
</tbody>
</table>

Reasons for Isolated HBcAb +

1. May be an indicator of chronic HBV infection where sAg has decreased to undetectable levels but DNA is detectable.
   - Seen in high prevalence regions and HIV +, HCV+
2. May be a marker of immunity after recovery from prior infection
3. May be a false positive test result
4. May be the only marker of infection during the window phase of acute hepatitis B; these persons should test positive for anti-HBc IgM.
Case 1
Mr. S. W.

- 52 yo Chinese-American man with known history HTN and hyperlipidemia transfers to you. His PMHx lists HBsAg+.
- Has no symptoms. Says he does not drink alcohol. Has had family tested, negative and vaccinated.
- What do you need to do as PCP?

Step 1 – History and Physical
- Risk factors for hepatitis B – vertical, household, sexual, IDU, occupational
- PMHx: Past clinical symptomatic hepatitis, DM, obesity, HCV, HAV, HIV
- Shx: Country of birth, country of parents’ birth, sexual history
- Fhx: HBV, Cirrhosis, HCC, alcohol, HCV
- Habits: alcohol, smoking, carcinogens

Step 2 – Establish state of viral replication
- AST, ALT
- HBV DNA PCR quantitative
- HBeAg
- Anti-Hbe
- HIV Ab
- HCV Ab

Step 3 – Establish state of liver disease
- Physical exam – stigmata of liver disease
  - Temporal wasting, abdominal fluid wave, splenomegaly, hepatomegaly, telangiectasias
- Tests of liver function: Albumin, INR
- Creatinine, INR, T bilirubin (MELD)
- Evidence of portal hypertension: Platelet count, ultrasound
Mr. S.W. results
- Mother had hepatitis B and father had HCC
- Wife and son are negative and vaccinated
- AST 32, ALT 35, Alk Phos 62, T Bili 0.9, Alb 4.1, Platelet 232, Cr 0.8, AFP 4.6
- HBV DNA 1,800 IU/mL
- HBeAg negative, anti-Hbe positive
- Ultrasound with echogenicity c/w fatty liver. Liver and spleen size normal.

S.W. – Assessment
Inactive Chronic hepatitis B
- NORMAL ALT
- HBV DNA < 2000 IU/mL
- HBeAg negative
- Lifelong infection probable

Groups Who Should be HBV Screened
- Born in areas of high prevalence or intermediate prevalence including immigrants and adopted children
- Household and sexual contacts of HBsAg + persons
- US born persons whose parents were born in regions of high HBV endemicity
- Ever injected drugs
- Multiple sexual partners or history of STDs
- Men who have sex with men
- Inmates of correctional facilities
- Persons needing immunosuppressive therapy
- Chronically elevated ALT or AST
- HCV or HIV infected
- Renal dialysis
- All pregnant women

CHB Prevalence Among Asian-Americans in San Francisco From 2001-2006
- Prevalence of chronic HBV infection among 3163 Asian American adults: 8.9%
  - Among chronically infected individuals, 65.4% were unaware of their serostatus
  - Among individuals without evidence of chronic infection, 44.8% showed no evidence of protective antibodies and, therefore, were at risk for future infection

Case 2
Mr. Q. H.

37 yo Asian male who has been living in the US for 10 yrs where he works as an engineer. Recently, he has been experiencing mild fatigue. PCP screens for HBV and he is positive for HBsAg.

Initial Workup – Results for Mr. Q.H.

- Hepatitis B e antigen (HBeAg) positive
- HBV DNA: $2.4 \times 10^8$ IU/mL
- HBV genotype: C
- ALT: 68 U/L (normal: 0-55 U/L)
- AST: 54 U/L (normal: 0-45 U/L)
- Platelet count: 189K
- Albumin: 4.6 g/dL
- Bilirubin: 0.9 mg/dL
- International normalized ratio: 1.1
- Creatinine: 0.8 mg/dL

Q.H. – Assessment:
Chronic hepatitis B

- Elevated ALT
- HBV DNA very high
- HBeAg positive
- Lifelong infection probable
Clinical Management of HBsAg+ Patient

- Determine hepatitis B status
  - Chronic eAg-positive hep B
  - Chronic eAg-negative hep B
  - Inactive chronic hep B
- Determine if treatment is needed
- Determine monitoring plan for patients not on treatment

Determining Treatment Candidacy for HBV

- Determining treatment candidacy at its most basic is a simple 2-step process of measuring
  - HBV DNA
  - ALT
- Also consider other parameters
  - Family history of HCC
  - eAntigen status
  - Liver biopsy – fibrosis stage
  - Coinfection with HIV or HCV

Frequent Recommended Monitoring for patients not on treatment (by AASLD)

**Inactive carriers**
- ALT every 6-12 months
- If ALT increases, then serial HBV DNA
- If HBV DNA >2000 serially, refer to consider liver biopsy

**Chronic HBV with normal ALT**
- ALT q 3-6 mo + HBV DNA and HBeAg q 6-12 mo
- If HBV > 20,000 and elevated ALT, refer for biopsy and/or treatment

Why Monitor So Often if Not on Treatment?

- Dynamic disease with changing states
- HBV DNA is the determining factor for treatment
- Frequent monitoring in order to capture right time for treatment
- Patients may have inactive disease for years and then reactivation is time for treatment
The Impact of Viral Load (DNA) in Hepatitis B

- Viral load significant factor in natural history of liver disease
  - prolonged immune destruction of antigen-presenting liver cells results in cirrhosis
  - prolonged low-level viremia may influence progression

- Viral load impacts risk of HCC
  - direct viral effect with replication and/or random integration can cause HCC

Cumulative Incidence of Liver Cirrhosis for Five HBV DNA Categories (n=3,774)

Cumulative Incidence of Decompensated Liver Cirrhosis (N=3774)

Measurements of HBV Treatment Effect

1. Reduction of HBV DNA level to undetectable level
2. HBeAg seroconversion
3. Normalization of ALT
**Two Patient Populations for Treatment**

**HBeAg-negative**
- Suppression of HBV DNA to undetectable
- ALT normalization

**HBeAg-positive**
- HBeAg loss and anti-HBe development (seroconversion)
- Suppression of HBV DNA to undetectable
- ALT normalization

**HBV Treatment Landscape**

**Primary Factors to Consider in HBV Therapy**

- Profile of drug resistance
- Presence of cirrhosis
- HIV coinfection
- Age of patient
- Prior treatment experience

**First line recommendations**
- Tenofovir, Entecavir, Peg Interferon

**Undetectable* HBV DNA After 1 Yr Of Treatment**

*By PCR-based assay (LLD ~ 50 IU/mL) except for some LAM studies.
### Other measures of Responses to HBV Antiviral Therapies in HBeAg positive patients

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Lamiv</th>
<th>Adefovir</th>
<th>Entecavir</th>
<th>Tenofovir</th>
<th>Telbivudine</th>
<th>PegIFN</th>
<th>PegIFN + Lam</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg convert</td>
<td>4-6%</td>
<td>16-21%</td>
<td>21%</td>
<td>21%</td>
<td>22%</td>
<td>27%</td>
<td>24%</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Na</td>
<td>Na</td>
<td>Na</td>
<td>Na</td>
<td>Na</td>
<td>Na</td>
<td></td>
</tr>
<tr>
<td>ALT Normal</td>
<td>7-24%</td>
<td>41-75%</td>
<td>77%</td>
<td>68%</td>
<td>68%</td>
<td>68%</td>
<td>39%</td>
</tr>
<tr>
<td>ALT</td>
<td>49-56%</td>
<td>53%</td>
<td>72%</td>
<td>74%</td>
<td>65%</td>
<td>38%</td>
<td>41%</td>
</tr>
<tr>
<td>Histol Improv</td>
<td>50-80%</td>
<td>90%</td>
<td>69%</td>
<td>Na</td>
<td>80%</td>
<td>Na</td>
<td>Na</td>
</tr>
</tbody>
</table>

### Comparison of Hepatitis B and C: Similar Tests, Different Meaning

<table>
<thead>
<tr>
<th>Hep B</th>
<th>Hep C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody</td>
<td>Vaccinated (sAb)</td>
</tr>
<tr>
<td>ALT</td>
<td>Indicates active disease, strong predictor of treatment response</td>
</tr>
<tr>
<td>Viral load</td>
<td>Predictor of cirrhosis and HCC</td>
</tr>
<tr>
<td>Genotype</td>
<td>Weak predictor of treatment response</td>
</tr>
<tr>
<td>Chronic</td>
<td>HBsAg positive</td>
</tr>
<tr>
<td>Resolved</td>
<td>sAg (-) sAb (+) cAb (+)</td>
</tr>
</tbody>
</table>

Lok, Hepatology, 2009