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

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Outline

1. Epidemiology of HCV and HBV
2. Approach to Hepatitis C Virus
   Natural History of HCV
   Initial Evaluation of Patient with HCV
   Long Term Management in Primary Care
   Current and Future HCV Treatments
3. Approach to Hepatitis B Virus
   Natural History of HBV
   Initial Evaluation of Patient with HBV
   Long Term Management in Primary Care
   Current HBV Treatments

Epidemiology of Hepatitis B and C
Epidemiology of Viral Hepatitis Worldwide and U.S. Disease Burden

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Worldwide</strong></td>
<td>40 mil</td>
<td>350 mil</td>
<td>170 mil</td>
</tr>
<tr>
<td>prevalence</td>
<td>0.2-0.5%</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td><strong>US</strong></td>
<td>0.94 mil</td>
<td>1.25 mil</td>
<td>4.1 mil</td>
</tr>
<tr>
<td>prevalence</td>
<td>0.2-0.5%</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td><strong>Deaths/Yr</strong></td>
<td>15,000</td>
<td>5,000</td>
<td>8-10,000</td>
</tr>
<tr>
<td><strong>Worldwide</strong></td>
<td>3.0 mil</td>
<td>500,000-750,000</td>
<td>250,000</td>
</tr>
</tbody>
</table>


Prevalence of HCV by Age and Race in US, 1988-94

Current and Future Complications of HCV in the U.S.
- HCV leading cause of death from liver disease and indication for transplant
- Prevalence decline expected by 2040
- As infected cohort ages, proportion with cirrhosis will increase 16% to 32% by 2020

**HCV Outcomes in Next 20 Years**

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


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**Epidemiology of HBV in the U.S.**

- 1980s: 430,000 new cases of HBV infection occurred each year in the U.S.
- 1997: 195,000 new cases of HBV infection per year in the U.S.

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**Chronic HBV Prevalence: Asian/Pacific Island Immigrants in NYC (2005)**

![Graph showing HBV prevalence by country of origin and years in the US.]


Prevalence of HCV and HBV Among HIV Patients

Prevalence of coinfection is influenced by geographic and ethnic origin

Hepatitis C Virus
Natural History and potential clinical outcomes in HCV

Hepatitis C Natural History Studies
- Limited prospective studies because of long course of disease and recent discovery
- Retrospective studies > prospective studies generally estimate higher proportion progress to cirrhosis, likely referral bias
- Multiple studies demonstrate the disease is not progressive in all patients
- Variables which influence disease progression are host and viral

Potential determinants of disease progression
- Alcohol
- Steatosis
- Male sex
- HBV coinfection
- Age at infection
- HIV, Immunosuppression
- HCV RNA – viral load
- HCV Genotype
- Mode of acquisition
- Ethnicity
- Duration
- ALT elevation
- Host genetic Determinants *
Groups Recommended for HCV Screening

- Injection drug use – ever, even if only used once
- HIV-infected individuals
- Hemophiliacs with clotting factors before 1987
- Hemodialysis recipients
- Unexplained aminotransferase abnormalities
- Transfusion or transplantation before July 1982
- Children born to women infected with HCV
- Healthcare, public safety, emergency medical personnel following needle injury or mucosal exposure
- Sexual partners with HCV-infected person


Algorithm for HCV Diagnostic Testing
Ab for screening, but not for diagnosis!

HCV Antibody
HCV RNA level

Chronic HCV Infection
- HCV Genotype

Spontaneous clearance of HCV
Likely
- HCV RNA qualitative to confirm

Or, false positive HCV Ab
Less likely
- Autoimmune disease
- HCV RIBA to confirm Ab

If suspect acute infection

If suspect false negative HCV Ab
- HIV, ESRD, immunocompromised

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, HBeAg, HAVAb
  - CBC, platelet, INR, Albumin, AST, ALT, Alkphos, Billirubin, 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 predicts 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

Qualitative and Quantitative RNA Testing

<table>
<thead>
<tr>
<th>Method</th>
<th>PCR</th>
<th>TMA</th>
<th>b-DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymerase</td>
<td>Transcription</td>
<td>Branching</td>
<td></td>
</tr>
<tr>
<td>chain reaction</td>
<td>mediated amplification</td>
<td>chain DNA</td>
<td></td>
</tr>
<tr>
<td>Qualitative</td>
<td>Qualitative</td>
<td>Quantitative</td>
<td></td>
</tr>
</tbody>
</table>

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HCV RNA and Liver Histology

Fibrosis

- Serum HCV RNA does not correlate with level of fibrosis

The Role of Ultrasound in Hep C

- Use to detect cirrhosis
  - enlarged spleen, small nodular liver, ascites, intraabdominal varices
- Use to detect HCC
- Cannot be used to determine fibrosis
- Helpful as a baseline assessment to determine if features suggestive of cirrhosis
- Not necessary for routine monitoring outside of cancer screening (cirrhotics only)

Hepatitis C Genotype

Role of a Liver Biopsy
Useful but Not Mandatory
- Why do we need to know about fibrosis?
  - Estimate risk for developing cirrhosis
  - Helps decision to delay or pursue treatment
  - Prognostic information
- Previously regarded as routine
  - Not required for HCV treatment consideration
- Stage scores: F0-F4
  - F0 = no scarring, F4 = cirrhosis
- Non-invasive fibrosis methods in the works

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

How do you interpret persistently normal ALT in hepatitis C?
- The spectrum of liver disease tends to be more mild in patients with normal ALT
- Yet, 14-24% of patients have fibrosis stage 2 or higher
- Progression of fibrosis still occurs
- Cirrhosis and liver failure still occur
Long Term Management of HCV Patients
What specifically should PCPs be doing?

- Monitor for development of cirrhosis
- Do not follow and reorder the HCV RNA
- Detection of extrahepatic conditions
- Long term follow up after HCV treatment
- Reassess for HCV treatment candidacy
- Management of cirrhosis
- Screening for HCC when advanced fibrosis-cirrhosis
- Appropriate referral for transplant – MELD score 8-10

Alcohol Counseling for Chronic Hepatitis C

- Alcohol use should be avoided or minimized
- > 50 grams per day increases fibrosis progression
- Alcohol consumption < 50 grams per day appears to increase HCV RNA level
- 50 grams of alcohol is approximately
  - 48 ounces of beer
  - 4.5 ounces of 80 proof
  - 15 ounces of wine.

1. Payrand T, Lancet. 1997;349:825-832
Hepatitis A and B Vaccination

- Hepatitis A vaccine should be given to non-immune patients
  - Fulminant HAV infection reported in persons with underlying chronic hepatitis C

- Hepatitis B vaccine should be given to susceptible patients (HBsAb - and HBeAb -)
  - Coinfection with hepatitis B and C accelerates progression to cirrhosis and HCC
  - Isolated HBeAb + controversial if vaccinate needed

Sexual Transmission of HCV?
Extremely Low Risk

- 776 serodiscordant spouses followed 10 yrs
  - Intercourse mean: 1.8/wk
  - No condom use, no anal sex
  - 3 new infections (incidence 0.37/1000 pt-yrs), but all 3 differed from partner's strain
  - Net incidence of transmission: 0

- Due to low sexual transmission rate, barrier protection not needed in monogamous relationships; otherwise, safe sex practices warranted


Extrahepatic Manifestations of HCV

Strong Evidence
- Porphyria cutanea tarda
- Membranoproliferative glomerulonephritis
- Cryoglobulinemia

Evidence more controversial
- B-cell lymphomas
- Diabetes mellitus
- Thyroid dysfunction
- Lichen planus
- Autoimmune / Biochemical markers
Antiviral Treatment of HCV
Pegylated interferon and ribavirin

- **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 for now**
  - Pegylated interferon and ribavirin
  - Genotype 1 = 48 weeks, Genotype 2,3 = 24 weeks

- **New drugs – Potentially in 2011**
  - Protease inhibitors and antiparasitic drugs.

Patterns of Response to Treatment

![Graph showing patterns of response to treatment]

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 8 yrs after treatment

But, Has HCV Treatment Been Shown to Better Clinical Outcomes?

Patients who achieved SVR -
1. Evidence of decreased rate of cirrhosis
2. Evidence of decreased rate of decompensation
3. Evidence of decreased rate of HCC
4. Evidence of decreased rate of liver related deaths

Shiratori, Annals of Int Med, 2005

Predictors of HCV Treatment Response

Positive
- Genotype 2 or 3
- Low Viral Load (<800,000 IU/L)
- Early virologic responders (EVR)
- Rapid virologic responders (RVR)
- Adherence:
  - >80% Tx duration
  - >80% IFN doses
  - >80% RBV doses

Negative
- Genotype 1
- High Viral Load (>800,000 IU/L)
- Cirrhosis
- Alcohol abuse
- Comorbidity
  - HIV
  - Hep B
  - High BMI

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

But what about all those side effects?

Side Effects

<table>
<thead>
<tr>
<th>PEG INTERFERON</th>
<th>RIBAVIRIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu-like, fatigue</td>
<td>Anemia, hemolytic</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Headache</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Cough</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Sore throat</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Depression</td>
<td>Birth defects</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Rash</td>
</tr>
<tr>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
</tr>
</tbody>
</table>
Ribavirin Rash

New Drugs for HCV

1. Protease inhibitors
   • Telaprevir, Boceprevir
   • Used only in combination with peginterferon ribavirin, otherwise resistance develops

2. Nitazoxanide
   • Anti-protozoal treatment
   • Also used for giardia, helminth and anaerobes

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 / relapsers: SVR 51-63% vs 14%

- SVR improved with boceprevir + PEG-IFN/RBV compared to PEG-IFN/RBV
  - Treatment naïve patients: SVR 67-75% vs 33%

Courtesy of Helen Yee, Pharm D, Alex Monto, M.D.
Hepatitis B Virus

Natural History of HBV:
Outcomes Depend on Age at Infection

Acute clinical illness
<5 y.o., <10%
>5 y.o., 30%-50%

Chronic infection:
<5 y.o., 30%-90%
>5 y.o., 2%-10%

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 (+)
Natural Course of Chronic HBV

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
Groups Who Should be HBV Screened

- Born in areas of high 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
- Men who have sex with men
- Inmates of correctional facilities
- Chronically elevated ALT or AST
- HCV or HIV infected, or persons needing immunosuppressive therapy
- Renal dialysis
- All pregnant women

Lok, AASLD Guidelines, Hepatology, 2009

Initial Evaluation of Patient with HBsAg+

Goals
1. Assess HBV replication status and activity/stage of liver disease to determine if antiviral treatment is indicated
2. Exclude other causes of liver disease
3. Counsel on prevention of transmission

Evaluation:
1. History and physical examination
2. Assessment of HBV replication: HBsAg, anti-HBc, quantitative HBV DNA
3. Assessment of liver disease: complete blood counts, hepatic panel, prothrombin time
4. Tests to rule out other causes of liver disease: anti-HCV, anti-HIV
5. Screening for HCC, AFP and ultrasound
6. Liver biopsy to grade and stage liver disease and to determine indications for treatment

Hepatitis B Serologic Markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Acute hepatitis B</th>
<th>Recovery from acute hepatitis B</th>
<th>Chronic HBeAg+ disease</th>
<th>Chronic HBeAg– disease</th>
<th>Successful vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBc IgM</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HBeAg</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>✓</td>
<td>(in some cases)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA (PCR if required)</td>
<td>✓ (may be only marker during chronic phase)</td>
<td></td>
<td></td>
<td></td>
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</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-HBe IgM.

HBV Genotypes

- 8 genotypes of HBV
- Labeled A-H
- Geographical variation, all genotypes seen in U.S. A = 35%, B = 22%, C = 31%
- Genotypes may be a factor in progression of liver disease and response to interferon tx

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
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

Monitoring HBV Patients in Primary Care
HBsAg+
- Are they chronic hepatitis B or inactive hepatitis B?
- Are they cirrhotic?
Chronic hepatitis B (high ALT, high DNA)
- Are they HBeAg (+) or HBeAg (-)?
- Are they high liver enzymes or normal?
- Are they high HBV DNA viral load or low?
- Are they appropriate for HBV treatment?
- Are they cirrhotic?
Inactive hepatitis B (normal ALT, very low DNA)
- Are they stable low level viral load and enzymes or do they have flares of high level DNA and enzymes?
- Are they cirrhotic?

Annual Rates of Disease Progression in Hepatitis B Infection
- HBeAg (+) chronic hep B
  - Cirrhosis: 5%
  - Decompensation: 3%
  - Decompensation: 2%
  - HCC: 0.4%
- HBeAg (-) chronic hep B
  - Cirrhosis: 1-2%
  - All HbsAg (+): 3%
  - HCC: 1%
From Highest to Lowest Risk of Progression to Cirrhosis and Complications

1. **Highest risk** = Chronic HBV with consistently elevated enzymes and high level HBV DNA
2. **Next highest risk** = Inactive chronic HBV but with flares of reactivation and enzyme elevation
3. **Lowest risk** = Inactive chronic HBV with persistently normal liver enzymes and low level DNA

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Long Term Management of HBV Patients

- Asian males 40 years of age or older
- Asian females 50 years of age or older
- All cirrhotic hepatitis B patients
- Family history of HCC
- Africans older than 20 years of age
- For noncirrhotic hepatitis B carriers not listed above, the risk still exists but varies depending on a number of factors

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HCC Surveillance Is Recommended for the Following Chronic HBV Patients

- Asian males 40 years of age or older
- Asian females 50 years of age or older
- All cirrhotic hepatitis B patients
- Family history of HCC
- Africans older than 20 years of age
- For noncirrhotic hepatitis B carriers not listed above, the risk still exists but varies depending on a number of factors

Counseling of Chronic HBV Patients

Goals:
1. Decrease rate of liver disease progression
2. Prevent transmission of infection

Strategies:
1. Hepatitis A vaccination
2. Decrease or stop alcohol consumption
3. Stop smoking, maintain ideal weight (healthy diet, regular exercise)
4. Practice safe sex, avoid sharing household articles that may be contaminated with blood (e.g., razors, toothbrushes, nail clippers)
5. Screen and vaccinate household members and steady sex partners

Aim of Antiviral Treatment for Chronic Hepatitis B

To prevent or delay the development of cirrhosis and hepatocellular carcinoma

Measurements of HBV Treatment Effect
1. Reduction of HBV DNA level to undetectable level
2. HBeAg seroconversion
3. Normalization of ALT
Objections to Early or Prolonged Therapy

- Development of resistance with nucleos (t)ide analogs
- Unknown side effects
- Can wait until the disease is active
- Ineffective if ALT is normal
- Cost

Recommendations for Treatment of HBeAg+ patients

<table>
<thead>
<tr>
<th>HBV DNA (copies/mL)</th>
<th>ALT</th>
<th>Treatment Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10⁷</td>
<td>Normal</td>
<td>No treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor every 6-12 months*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider therapy in patients with known significant histologic disease, even if low-level replication</td>
</tr>
<tr>
<td>≥ 10⁷</td>
<td>Normal</td>
<td>Low rate of HBeAg seroconversion for interferon, lamivudine, adefovir, and probably entecavir and peginterferon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider peginterferon if disease is evident</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If needed, lamivudine, adefovir, or entecavir preferred (more potent HBV suppressive agents with fewer side effects)</td>
</tr>
<tr>
<td>≥ 10⁷</td>
<td>Elevated</td>
<td>Adefovir, lamivudine, entecavir, peginterferon, or interferon are first-line options</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&quot;High&quot; HBV DNA (≥10⁷), adefovir, lamivudine, or entecavir preferred</td>
</tr>
</tbody>
</table>

*Upon initial diagnosis, every 3 months for 1 year to ensure stability |
With permission and modified from Freysz, et al.**

Recommendations for Treatment of HBeAg - patients

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<tr>
<td>≥ 10⁷</td>
<td>Normal</td>
<td>Low efficacy for lamivudine, interferon, adefovir, entecavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider peginterferon, if disease</td>
</tr>
<tr>
<td>≥ 10⁷</td>
<td>Elevated</td>
<td>Adefovir, lamivudine, entecavir, peginterferon, or interferon are first-line options</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Long-term treatment required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adefovir or entecavir preferred (low rate of resistance)</td>
</tr>
</tbody>
</table>

*Upon initial diagnosis, every 3 months for 1 year to ensure stability |
With permission and modified from Freysz, et al.**
### HBV Treatment and Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Lamivudine (n=436)</th>
<th>Placebo (n=215)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall disease</td>
<td>34 (7.8)</td>
<td>38 (17.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Progression, n(%)</td>
<td>15 (3.4)</td>
<td>19 (8.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Increase in Child's</td>
<td>17 (3.9)</td>
<td>16 (7.4)</td>
<td>0.47</td>
</tr>
<tr>
<td>score, n(%)</td>
<td>2 (0.5)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>HCC, n(%)</td>
<td>17 (3.9)</td>
<td>16 (7.4)</td>
<td>0.47</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2 (0.5)</td>
<td>3 (1.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Advantages and Disadvantages of HBV Drugs

<table>
<thead>
<tr>
<th>Agent</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon</td>
<td>+ High Ylcs&lt;br&gt;+ Short Treatment Duration&lt;br&gt;+ No resistance</td>
<td>+ Parenteral Administration&lt;br&gt;+ Poor Tolerance</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>+ Oral Administration&lt;br&gt;+ Excellent Tolerance&lt;br&gt;+ Use in ESLT&lt;br&gt;+ Use in Anterior Tissue</td>
<td>+ Drug resistance common (~20% yr)</td>
</tr>
<tr>
<td>Adefovir</td>
<td>+ Oral Administration&lt;br&gt;+ Excellent Tolerance&lt;br&gt;+ Use in ESLT&lt;br&gt;+ Use in Anterior Tissue</td>
<td>+ Drug resistance, through uncommon (0% at year 1, ~7% at year 2, 7% at year 3, 13% at year 4)</td>
</tr>
<tr>
<td>Entecavir</td>
<td>+ Oral Administration&lt;br&gt;+ Excellent Tolerance&lt;br&gt;+ Use in ESLT&lt;br&gt;+ Use in Anterior Tissue</td>
<td>+ Drug resistance uncommon (0% at year 1, resistance mutations noted in previously lamivudine-resistant patients)</td>
</tr>
<tr>
<td>Peginterferon</td>
<td>+ High Ylcs&lt;br&gt;+ Fixed Duration of Treatment&lt;br&gt;+ No Drug resistance</td>
<td>+ Parenteral Administration&lt;br&gt;+ Tolerance better than interferon but less than end agents</td>
</tr>
</tbody>
</table>

### Indications for HBV Vaccination in Adults

- **HIV infection**
- **Chronic liver disease**
- **End-stage renal disease**
- At risk of occupational exposure
- Household contacts or sex partner of persons with HBV
- illegal injection drug use – current or recent
- Sexually active persons with multiple partners
- Men who have sex with men
- Travelers to regions of high-intermediate HBV prevalence
- Seeking evaluation or treatment for a STD

CDC. MMWR Morb Mortal Wkly Rep. October 19, 2007 / 56(41);Q1-Q4
Comparison of Hepatitis B and C
Similar Tests, Different Meaning

<table>
<thead>
<tr>
<th></th>
<th>Hep B</th>
<th>Hep C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody</td>
<td>Vaccinated (sAb)</td>
<td>Exposed (HCV Ab)</td>
</tr>
<tr>
<td>Exposed (sAb + cAb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>Indicates active</td>
<td>Does not determine</td>
</tr>
<tr>
<td></td>
<td>disease, strong</td>
<td>active disease, not</td>
</tr>
<tr>
<td></td>
<td>predictor of treatment</td>
<td>predictor of treatment</td>
</tr>
<tr>
<td></td>
<td>response</td>
<td>response</td>
</tr>
<tr>
<td>Viral load</td>
<td>Predictor of cirrhosis</td>
<td>No correlation w/</td>
</tr>
<tr>
<td></td>
<td>and HCC</td>
<td>cirrhosis or HCC</td>
</tr>
<tr>
<td>Genotype</td>
<td>Weak predictor of</td>
<td>Strong predictor of</td>
</tr>
<tr>
<td></td>
<td>treatment response</td>
<td>treatment response</td>
</tr>
<tr>
<td>Chronic</td>
<td>HBsAg positive</td>
<td>HCV RNA positive</td>
</tr>
<tr>
<td>Resolved</td>
<td>sAg (-) sAb (+) cAb (+)</td>
<td>Ab (+) qualitative RNA (-)</td>
</tr>
</tbody>
</table>

Practice Guidelines and Resources
- VA National Hepatitis C Program
  www.hepatitis.va.gov
- CDC: Viral Hepatitis
  www.cdc.gov/ncidod/diseases/hepatitis
- American Liver Foundation
  www.liverfoundation.org
- American Association for the Study of Liver Diseases
  www.aasld.org