Inactive HBsAg+ Carrier State

Justine Lee, M.D.
Medical Director
New York Life Insurance Company
MUD Group January 2011
New York Life adheres to the letter and spirit of the antitrust laws. The information in this lecture is intended to advance the knowledge and improve the risk assessment skills of the participants. Under no circumstances shall this lecture be used as a forum for the pricing of specific products, determining how they are marketed, or any other anticompetitive purpose.

Copyright 2011 New York Life Insurance Company. All rights reserved.
Objectives

- Abbreviations
- Vital Statistics
- Diagnostic Criteria
- Routes of Transmission
- Natural History
- Subtypes of Hepatitis B carriers
HBV Antigen Testing

• HBsAg – Hepatitis B surface antigen

• HBeAg – Hepatitis B e antigen
HBV Antibody Testing

- HBsAb – Hepatitis B surface antibody
- Anti-HBe – Antibody to e antigen
A simplified drawing of the HBV particle and surface antigen
HBV Viral Load

• HBV DNA
  – IU/ml
  – Copies/ml
HBV Testing

• HBsAg+ = infection
  – Cannot determine inactive carrier state vs. chronic infection from this single test

• HBsAb+ = immunity
Terminology

• Previous
  – Healthy carrier

• Current
  – Inactive HBsAg+ carrier
• Estimated 350 – 400 million persons are chronically infected with HBV, worldwide.
Geographic Distribution

Prevalence of chronic infection with HBV, 2006 CDC
• Estimated 5 – 7 million persons chronically infected with HBV and HCV in U.S.

• Estimated two thirds of these individuals are not aware of infection.
Diagnostic Criteria

• Chronic Hepatitis B
  – HBsAg positive >6 months
  – Serum HBV DNA >20,000 IU/ml
  – Persistent or intermittent elevation in AST/ALT
  – Liver biopsy showing chronic hepatitis with moderate or severe necroinflammation
Diagnostic Criteria

- **Inactive Carrier State**
  - HBsAg positive > 6 months
  - HBeAg-, anti-HBe+
  - HBV DNA < 2,000 IU/ml
  - Persistently normal AST/ALT
  - Liver biopsy confirms absence of significant hepatitis
Routes of Transmission

• Developing Countries
  – Perinatally acquired
  – Person to person during childhood

• Developed Countries
  – Usually acquired during adulthood through sexual transmission and injection drug use.
Risk of HBV Infection After Acute Exposure

• 90% in newborns of HBeAg+ mothers

• 25 – 30% in infants and children under 5

• < 5% in adults
Natural History of HBV Infection

• In perinatally acquired infection, large percentage of HBeAg+ patients have high serum HBV DNA but normal ALT levels

• Considered to be in “immune tolerant” phase

• Clearance of HBeAg is much lower in these patients.
• HBV acquired during childhood is usually person to person.

• Most children who are HBeAg+ have elevated ALT levels.

• Seroconversion to Anti-HBe is common near or shortly after onset of puberty.
• After spontaneous HBeAg seroconversion, 67% to 80% of carriers have low or undetectable HBV DNA and normal ALT levels with minimal or no necroinflammation on liver biopsy - the “inactive carrier state”.

• Roughly 10% - 20% of inactive carriers may have reactivation of HBV replication and exacerbation of hepatitis after years of quiescence.
Subtypes of HBsAg+ Carriers

- Study by Simons and colleagues from Alaska
- 97 chronically infected Alaskan natives
- Persistently normal ALT levels
- Low level HBV DNA
- Followed for several years
Subtypes of HBsAg+ Carriers

- In these 97 patients, 3 patterns of activity:
  - steady low level replicative state
  - Fluctuating replication with a change in HBV DNA levels in a magnitude of 2-3 logs
  - Persistently negative HBV DNA
Subtypes of HBsAg+ Carriers

• The 3rd group with an absence of HBV DNA during the follow-up period, went onto lose HBsAg in a significant number.

• 14 out of the 16 patients who lost HBsAg came from the group with persistently negative HBV DNA.
Subtypes of HBsAg+ Carriers

- Even within the inactive carrier state, there are subsets of patients whose prognosis differs.

- Crucial to determine whether there is complete absence of HBV DNA as this seems to predict high likelihood of ultimate clearance of HBsAg.
Risk Factors for Progression in Carriers

- Presence of HBeAg and high levels of HBV DNA were independent risk factors for subsequent development of cirrhosis and HCC.
Summary

• HBsAg+ alone is insufficient to differentiate between inactive carrier state vs. chronic active infection.

• ALT levels are persistently normal in inactive HBsAg+ carrier state.

• If HBV DNA levels are available, persistent undetectable HBV DNA levels for several years appears to define HBsAg+ inactive carrier with best prognosis.
References

- AASLD Practice Guideline Update: Chronic Hepatitis B, Update 2009
- Medscape- Abstract by Simons and colleagues from AASLD Conference 2010, Boston, MA.