



Inactive HBsAg+ Carrier State

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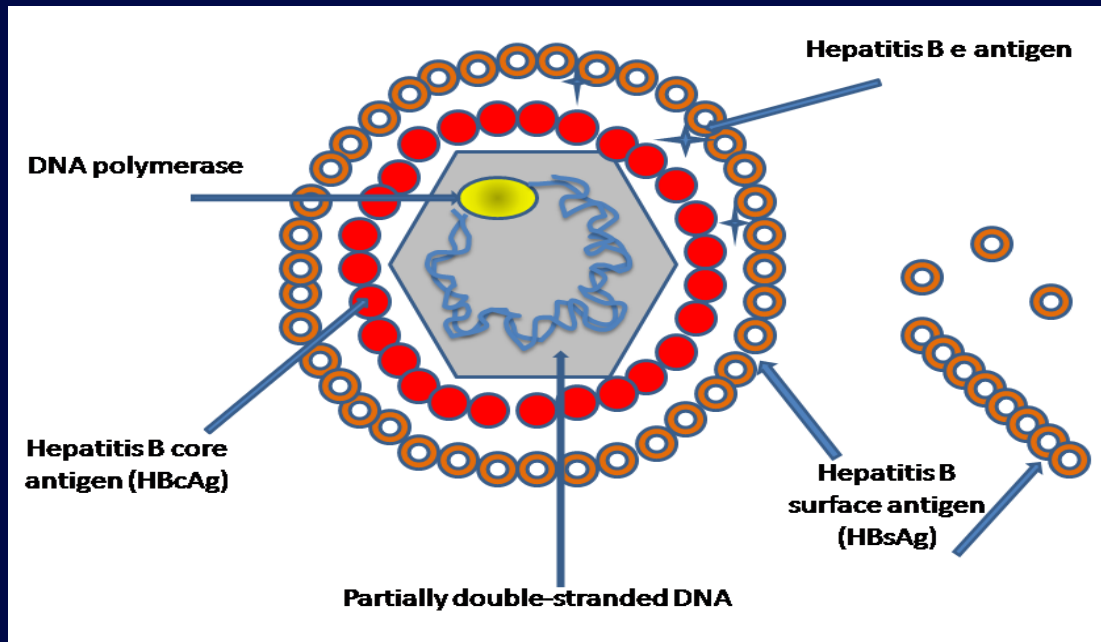
- Abbreviations
- Vital Statistics
- Diagnostic Criteria
- Routes of Transmission
- Natural History
- Subtypes of Hepatitis B carriers

HBV Antigen Testing

- HBsAg – Hepatitis B surface antigen
- HBeAg – Hepatitis B e antigen

- HBsAb – Hepatitis B surface antibody
- Anti-HBe – Antibody to e antigen

Diagram of HBV Virus



A simplified drawing of the HBV particle and surface antigen

- HBV DNA
 - IU/ml
 - Copies/ml

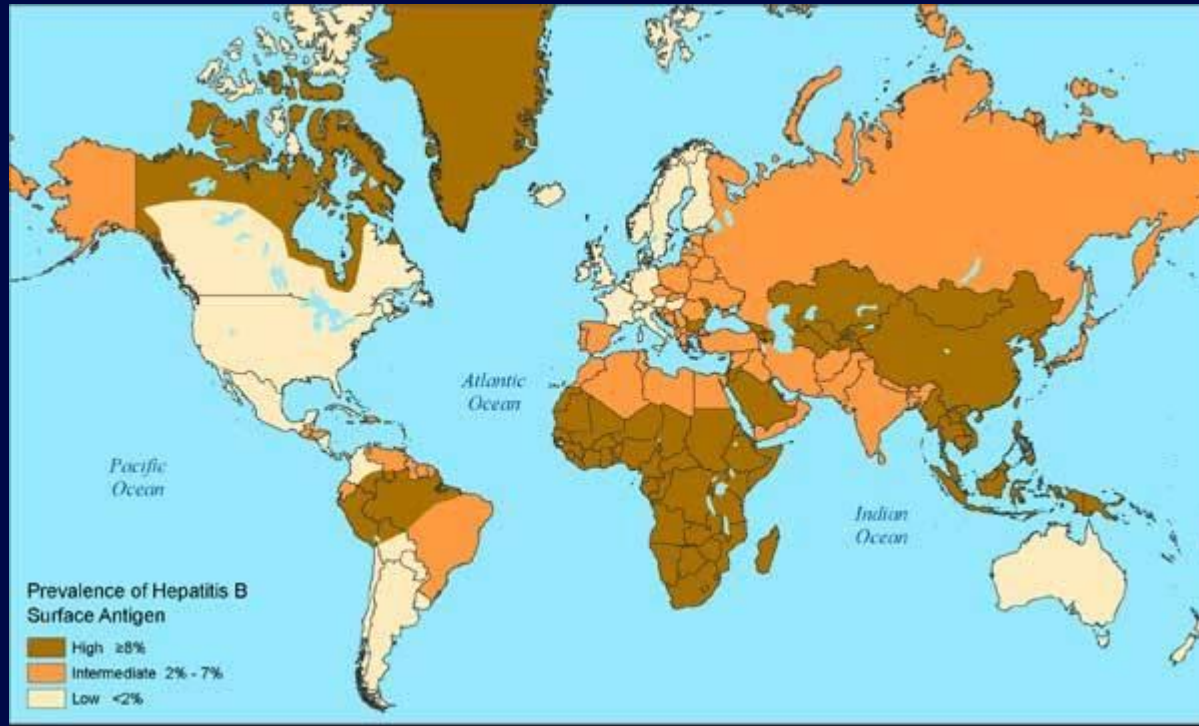
- HBsAg+ = infection
 - Cannot determine inactive carrier state vs. chronic infection from this single test
- HBsAb+ = immunity

- 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.

- 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

- 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

- Developing Countries
 - Perinatally acquired
 - Person to person during childhood
- Developed Countries
 - Usually acquired during adulthood through sexual transmission and injection drug use.

- 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.

Natural History of HBV Infection

- 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.

- 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.

- AASLD Practice Guideline Update: Chronic Hepatitis B, Update 2009
- J Viral Hepatology 2008; 15(6): 434-441
- Medscape- Abstract by Simons and colleagues from AASLD Conference 2010, Boston, MA.



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