



# **Guide for the Identification and Management of Chronic Hepatitis B in Primary Care Setting**

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# **AASLD and the Hepatitis B Special Interest Group Thank the Following for Their Contribution in Providing Peer Review of This Slide Module:**

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# Objectives

- Rational for Screening for HBV
- Outline risk factors for HBV
- Discuss initial management of persons who test positive for HBsAg
- Discuss initial PCP management
  - whom to follow and whom to refer
- Case illustration at end to highlight important teaching questions



# Nomenclature

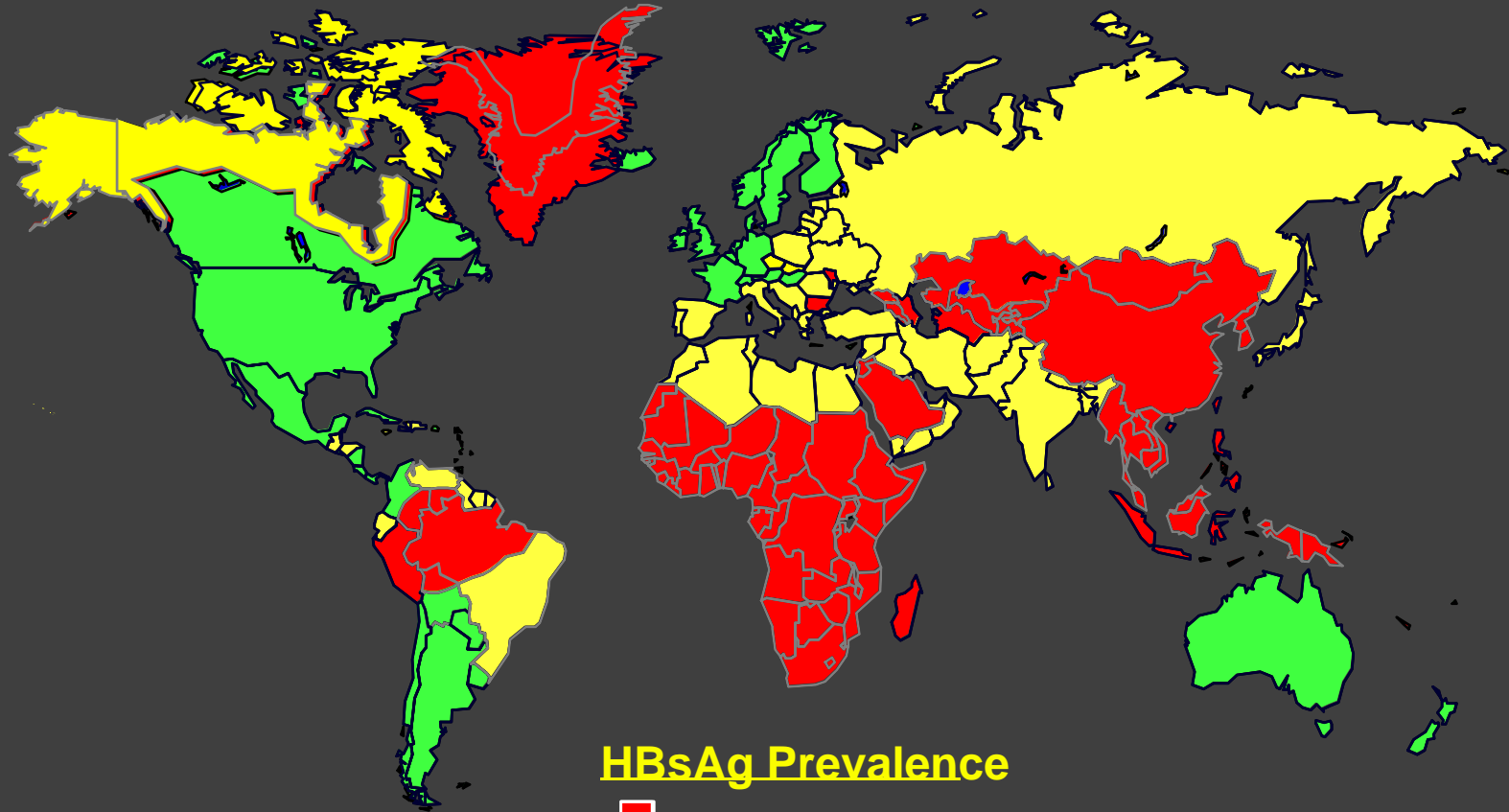
- HBV: Hepatitis B virus
- HBsAg: hepatitis B surface antigen
  - marker of active infection
  - Chronic hepatitis B: HBsAg positive for at least 6 months
- Anti-HBs (or HBsAb): Antibody to HBsAg
  - marker of immunity to hepatitis B
- HBeAg: hepatitis B “e” antigen
  - surrogate marker of high viral load
- Anti-HBe: antibody to HBeAg
  - associated with lower viral load
- HBV DNA: Presence means active viral replication



# Who Should Be Tested For HBV Infection?

- Individuals from countries where prevalence is  $\geq 2\%$
- Blood and organ donors
- Hemodialysis patients
- Pregnant women
- Infants of HBsAg + mothers
- Behavioral contacts: see slide 11 for other groups
  - Sexual contacts
    - HIV+, homosexual males, injecting drug users
- Patients receiving immunosuppressive therapy
- Abnormal ALT of unknown cause

# Geographic Distribution of Chronic HBV Infection



## HBsAg Prevalence

- 8% - High
- 2-7% - Intermediate
- <2% - Low

# Association Between Age and Development of Chronic HBV Infection

- Risk of developing chronic infection is age dependent
- Occurs more frequently in younger age groups

## Age Group

Newborns & infants

Children 1-5 years old

Adolescents and adults

## Chronic Infection

90 %

25-30 %

<5%

Risk of chronic infection higher in immune suppressed individuals  
Including those on hemodialysis or with HIV infection

# HBV Infection in Asian/Pacific Islanders in the US

- Worldwide 75% with chronic HBV are Asians
- In US annually there are ~100,000 new infections, 8,000 - 32,000 chronic infections, and 5,000 - 6,000 deaths
- Prevalence of chronic hepatitis B
  - Less than 1 in 2000 in the US population
  - 1 in 10 among Asian Americans (most are untested and unaware of their disease)
- Chronic HBV infection in Asians is associated with 25% lifetime risk of HCC or death due to cirrhosis

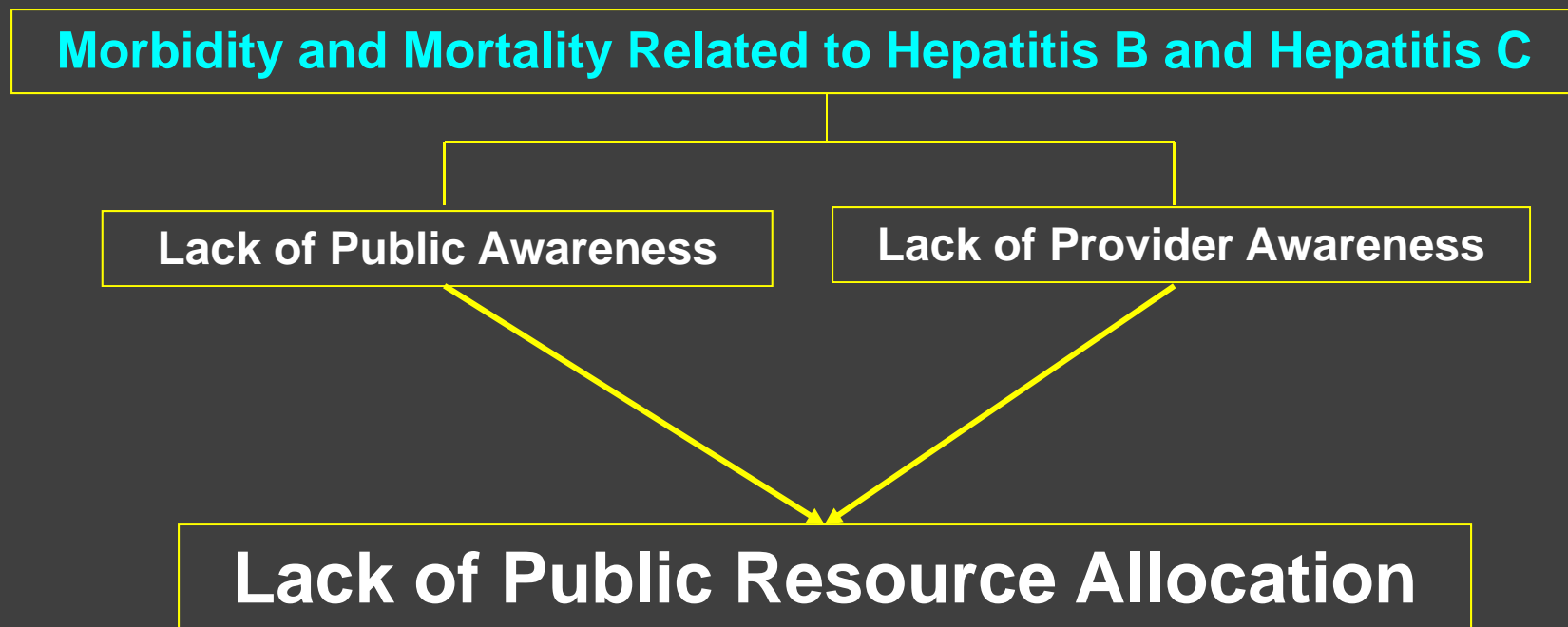
# Adult Indications for HBV Screening and/or Vaccination: Persons at Risk for Infection

<b>Behavioral</b>	IV drug users; more than 1 sex partner in previous 6 months; recently acquired STD, including all clients in STD clinics; men who have sex with men
<b>Occupational</b>	Health professionals; public safety workers with exposure to blood
<b>Other Contacts</b>	sex partners of persons with chronic HBV; clients, staff in institutions for developmentally disabled; correctional facility inmates; travelers for >6 months to countries with high or intermediate ( $\geq 2\%$ ) prevalence of HBV, HIV or HCV infection
<b>Medical</b>	Hemodialysis; receiving clotting factor concentrates

# NIH Consensus Conference and Institute of Medicine Recommendations

- Burden of HBV is high in US
- More comprehensive screening by PCPs for HBV is needed for evaluation, vaccination, management and/or referral
- Treatment of appropriate candidates:
  - Improves clinical outcome and liver disease
  - Decreases long-term risk of liver decompensation
  - Possibly decreases hepatocellular carcinoma

# The Institute of Medicine Findings 2010



# The Consequences

## Morbidity and Mortality Related to Hepatitis B

Lack of Public Awareness

Lack of Provider Awareness

Lack of Public Resource Allocation

- At-risk people do not know how to prevent becoming infected
- At-risk people may not have access to preventive services
- Chronically infected people do not know that they are infected
- Providers do not screen people
- Providers do not know how to manage infected patients
- Inadequate access to testing and medical management
- Inadequate disease-surveillance systems

From IOM Report 2010

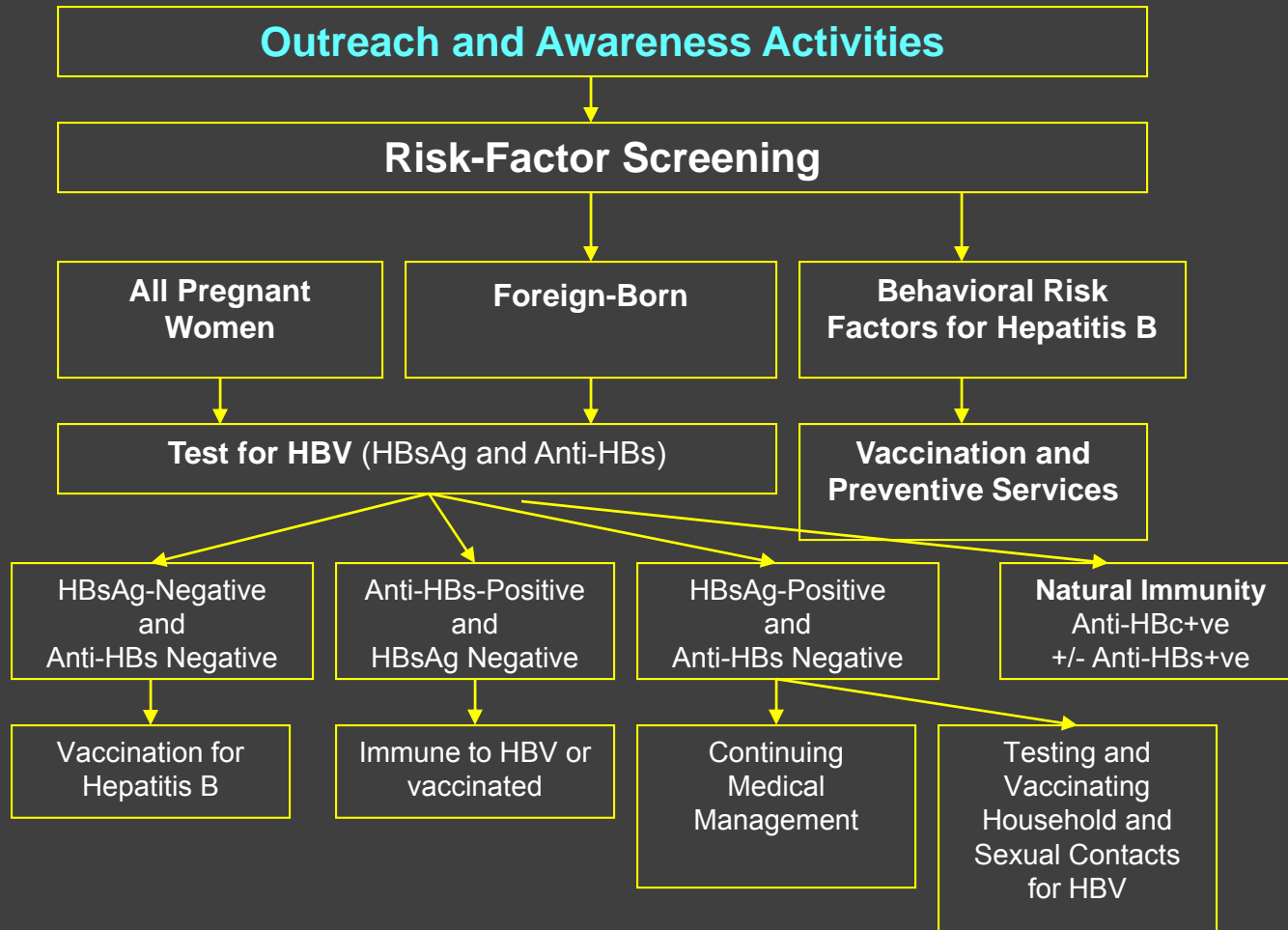
# Provider and Community Awareness Findings

- Health-Care and Social-Service Providers
- Low levels of knowledge about hepatitis B
  - Prevalence and incidence
  - Who is at risk
    - Chronic vs. acute
    - Who to test?
    - Who to vaccinate?
  - Interpretation of test results
  - Clinical sequelae
  - Medical management for chronic infection
- General and At-Risk Community
- Low awareness within general community
- Low awareness within at-risk communities
- Stigma: Some Asian Countries may discriminate against persons with HBV by disqualifying them from employment. Hence fear about testing
- Limited educational programs

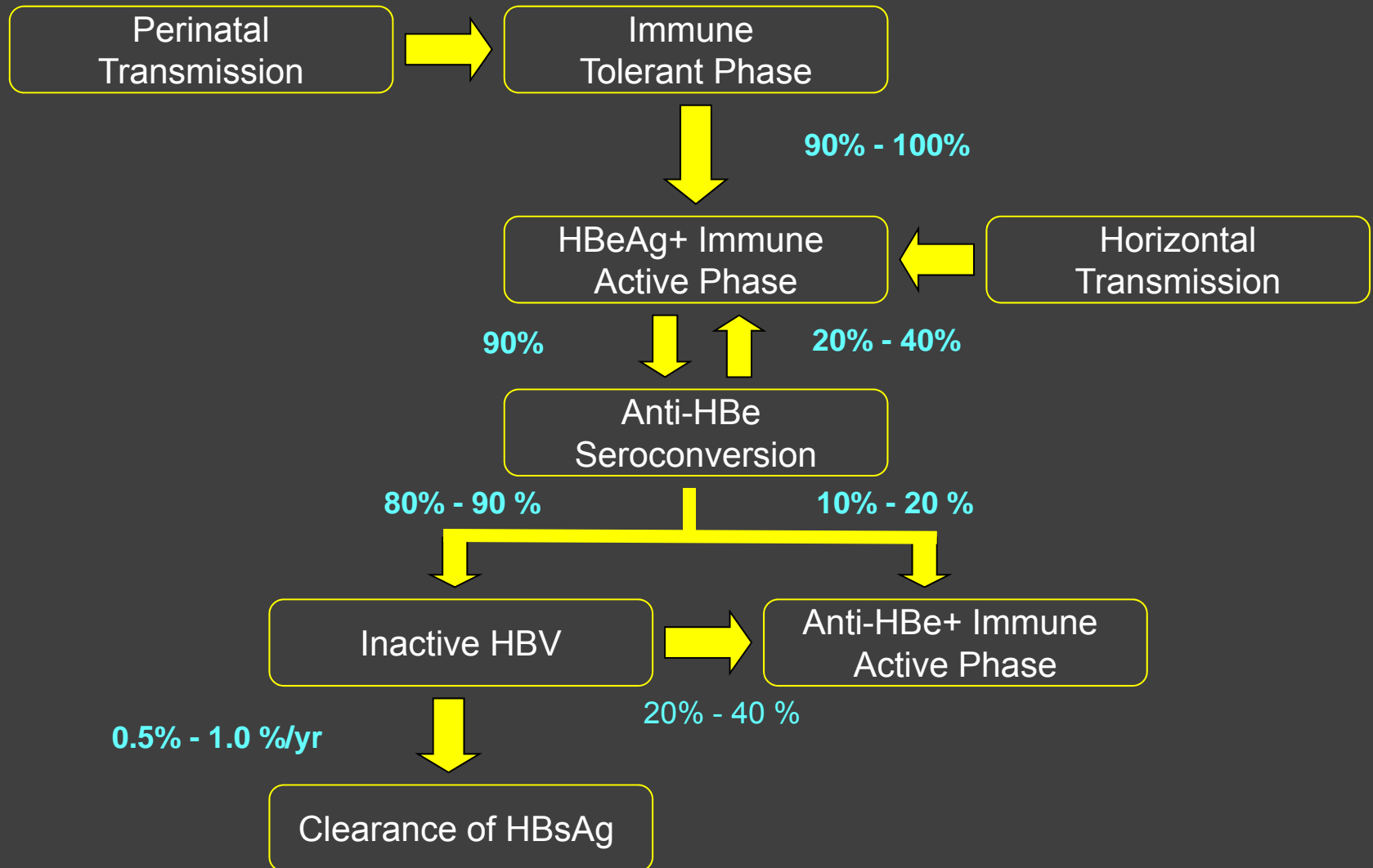
# Provider and Community Awareness Findings (cont.)

- Health-Care and Social-Service Providers
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- Stigma: In Some Asian Countries having HBV disqualifies persons for employment and they can be discriminated against: Hence fear about testing
- Limited educational programs

# Model for Viral Hepatitis B Services



# Natural Progression of Chronic HBV Infection



# PCP in Initial Evaluation and Management of HBsAg+ Patient

- Chronic HBV Infection
  - HBsAg+ for at least 6 months
- Initial evaluation: H & P, complete liver panel, HBeAg and anti-HBe, HBV DNA, Plt count
- Assess phase of patient (see next slide)
- Do US of liver every 6 months to detect HCC at treatable stage
  - If patient male over 40 or female over 50 years of age
  - In male African nationals over the age of 20
  - If patient has cirrhosis or family history of HCC
- Educate patient, test family and sexual contacts

# Phases of Chronic HBV: Role of PCP

<i>Phase</i>	<b>HBeAg/ anti-HBe</b>	<b>ALT level</b>	<b>HBV DNA</b>	<b>Liver biopsy</b>	<b>PCP Action</b>
<b>Immune Tolerant</b>	HBeAg+	normal	> 1 million IU/ml	No or minimal activity	Follow ALT every 3-6 months: refer if ALT >ULN
<b>Immune Active</b>	Either HBeAg+ or negative	Elevated	> 2,000 IU/ml	Mild to severe disease	Refer to Specialist
<b>Inactive</b>	HBeAg negative, anti-HBe positive	normal	< 2,000 IU/ml	Mild or minimum activity +/- inactive cirrhosis	Monitor ALT every 6 months, if ALT elevated do HBV DNA, refer if both are elevated

# Case Presentation

- 35 y.o. Chinese male, BMI 30, born in Singapore is asymptomatic. At local Health Fair ALT found to be 45 (ULN 40) . Presents to his primary care physician of 3 years. The first thing his doctor should do is:
  - A. Do liver US to look for fatty liver
  - B. Refer for liver biopsy
  - C. Follow-up ALT in 6 months to 1 year
  - D. Screen for hepatitis B (HBsAg and anti-HBs)



# Case Presentation

- The correct answer is D: Screen for hepatitis B with testing for both HBsAg and anti-HBs.
- Liver US does not confirm etiology of abnormal liver tests or extent of disease unless very advanced
- Liver biopsy is invasive and is not indicated at this point.
- Further follow up is unlikely to provide additional useful information

# Case Presentation (cont.)

- The PCP should next:
  - A. Refer for liver biopsy
  - B. Do H & P and further lab tests
  - C. Tell patient to isolate himself from co-workers
  - D. Screen family and sexual contacts for HBsAg and anti-HBs and vaccinate those who test negative
  - E. B and D are correct



# Slide Presentation (cont.)

- Correct answer is E: H&P, labs, screen
- Initial laboratory tests should include:
  - HBeAg and anti-HBe
  - Full liver function test panel
  - CBC to assess platelet function (if  $<100,000$  suggests cirrhosis with splenomegaly)
  - HBV DNA level: If level is greater than 2,000 IU/mL refer to liver specialist for evaluation
- Educate patient about HBV and screen family and sexual contacts

## Case Study (cont.)

- Patient returns every 3-6 months. ALT WNL for 18 months. At year 2 ALT 273 U/L. He remains asymptomatic. The provider should
  - A. Treat immediately with antiviral medication
  - B. Do a liver biopsy
  - C. Refer to a liver specialist
  - D. Advise him to start herbal remedies

# Case Presentation (cont.)

- Correct answer is C: Refer to liver specialist
- Specialist correctly elects to wait 6-12 months to see if HBeAg seroconversion occurs spontaneously since patient has no stigmata of liver disease and platelets, bilirubin and albumin are all WNL--
  - 6 months later ALT is 22, HBeAg is negative and anti-HBe is positive
  - HBV DNA is 500 IU/ml
- Patient is sent back to PCP for follow-up q 3-6 months ALT with HBV DNA every 6 months

## Case Presentation (cont.)

- Patient is carefully followed with ALT/AST q. 6 months. 3 years later ALT increases to 120 U/L. HBV DNA is 80,000 IU/ml.

Correct next step is:

- A. Start lamivudine 100 mg daily
- B. Start entecavir or tenofovir
- C. Wait to see if ALT improves spontaneously
- D. Refer for liver transplant
- E. Refer to liver specialist for possible liver biopsy and evaluation for treatment

# Case Presentation (cont.)

- Correct answer E. The specialist performs a liver biopsy which shows early bridging fibrosis and moderate hepatitis.
- Liver specialist starts entecavir or tenofovir
  - Specialist monitors ALT and HBV DNA every 3 months. ALT remains < 30 and HBV DNA is undetectable after 3 months and remains so for 2 years.
  - Specialist sends patient back to PCP to monitor ALT and HBV DNA every 6 months and re-refer if either become elevated
- Patient education – need for compliance and side effects

# Key Learning Points

- PCP should play major role in screening high risk persons for hepatitis B and their contacts
- PCP should vaccinate high risk susceptible persons
- PCP should test family members and sexual contacts of HBsAg positive patients
- PCP should test for HBsAg in all patients who are scheduled for cancer chemotherapy, anti-TNF therapy (e.g. rheumatoid arthritis, IBD), rituximab or likely to be on chronic or intermittent corticosteroids.

# Key Learning Points (cont.)

- PCP can perform initial evaluation and laboratory tests for HBsAg+ persons
- PCP can follow chronic HBV infected persons in immune tolerant or inactive phases of HBV
- PCP should refer persons in immune active phase to a specialist
- PCP should confer with a liver specialist to ensure that those who have underlying liver disease are treated appropriately.