

Summary of

***“Recommendations for Identification and
Public Health Management of Persons
with Chronic Hepatitis B Virus Infection”***

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Rationale for Release of New Recommendations

- Recent improvements in treatment for chronic HBV infection increase the importance and benefit of prompt diagnosis
- Screening and vaccinating close contacts of HBV-infected persons will help reduce the burden of disease
- When fully implemented, chronic hepatitis B testing and public health management will significantly reduce morbidity and mortality associated with chronic HBV infection

Burden of Disease

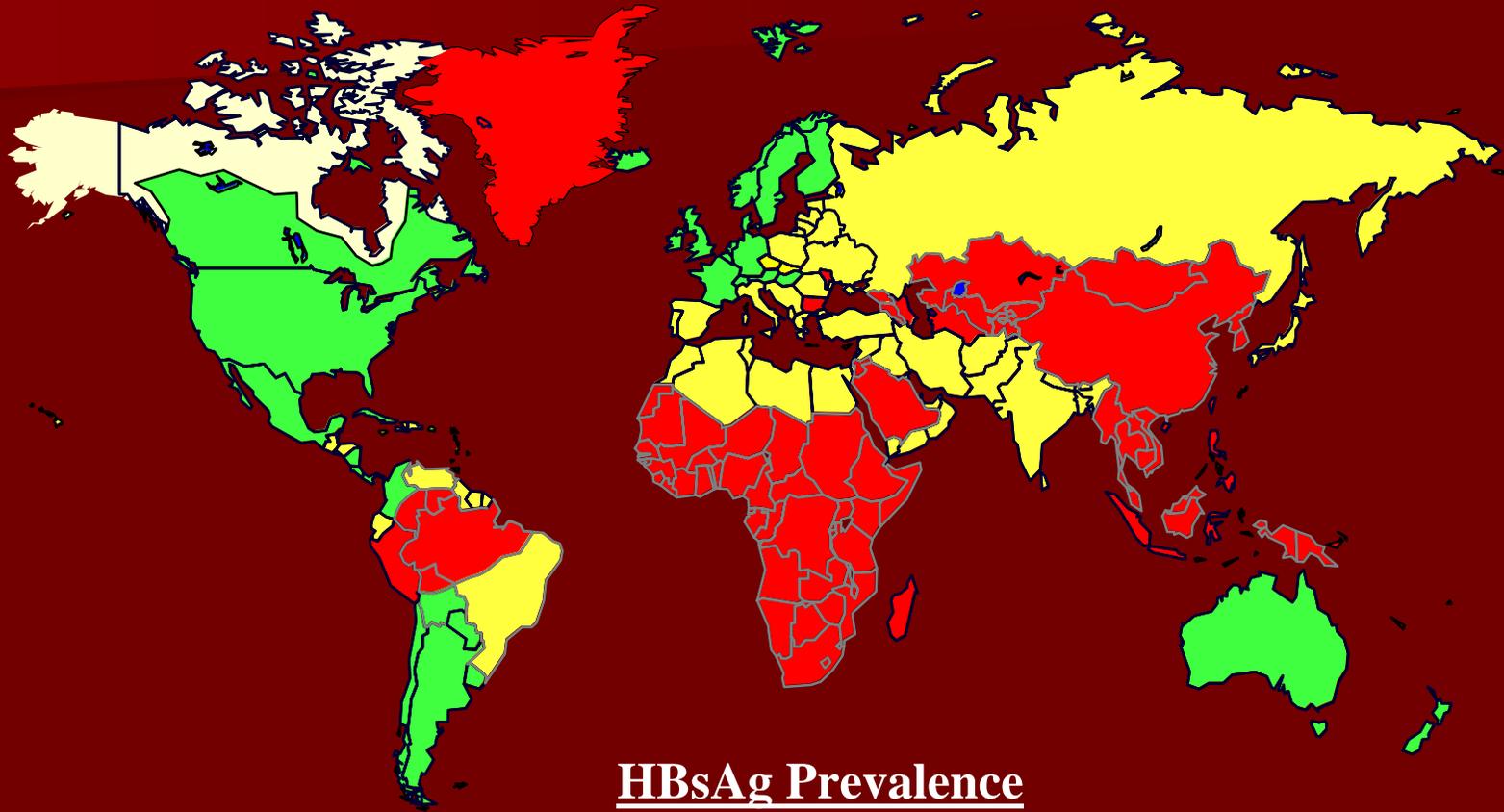
United States

- In 2006
 - approximately 800,000 to 1.4 million residents were living with chronic HBV infection
 - 46,000 newly infected
- Underlying cause of death for 2,000-4,000 people annually

Worldwide

- 350 million have chronic HBV infection
- 620,000 die annually from HBV-related liver disease

Geographic Distribution of Chronic HBV Infection



HBsAg Prevalence

- $\geq 8\%$ - High
- 2-7% - Intermediate
- $< 2\%$ - Low

Who Should Be Screened

Previously Recommended

- Pregnant women
- Infants born to mothers positive for Hepatitis B surface antigen (HBsAg)
- Household contacts and sex partners of HBV-infected persons
- People born in countries with prevalence $> 8\%$ and their US born children
- Source patients in occupational exposure
- People with HIV

2008 Expanded Recommendations

- Men who have sex with men
- Injection drug users
- People born in countries with prevalence $>2\%$
- People receiving cytotoxic or immunosuppressive therapy
- People with unexplained liver disease

In the US, routine testing for chronic hepatitis B is now also recommended for:

- People born in Asia, Africa, and other geographic regions with a prevalence of chronic HBV infection greater than or equal to 2% (including immigrants, refugees, asylum seekers and internationally adopted children);
- Unvaccinated people who were born in the U.S. and whose parents are from highly endemic regions;
- Men who have sex with men;
- Injection drug users; and
- People with selected medical conditions, including abnormal liver function tests not explained by other factors and people who require immunosuppressive therapy

Vaccinate at Time of Testing

- Don't wait to vaccinate
- Provide first dose of vaccine and test during same visit (unless existing provider-patient relationship ensures return visit)
- Especially important in settings where universal vaccination is recommended
 - STD clinics, HIV testing sites, drug abuse treatment and prevention settings, health care settings for IDUs, health care settings for MSM, correctional facilities
- Provide vaccination even if screening is not feasible

Chronic HBV Meets the Criteria for Public Health Screening

- Chronic HBV is a serious health disorder that can be diagnosed before symptoms occur
- Can be detected by reliable, inexpensive and minimally invasive screening test
- Patients can gain years of life if evaluation/ treatment is initiated early
- Cost is reasonable compared to benefits

Laboratory Testing

- Use a serologic assay for Hepatitis B surface antigen (HBsAg) that is FDA- licensed or approved
- Perform test in accordance to manufacturer's guidelines
- Test initially reactive specimens with a licensed confirmatory test
- Chronic infection is confirmed by the absence of IgM antibody to Hepatitis B core antigen (IgM anti-HBc) or the persistence of HBsAg or HBV DNA for at least 6 months

Comparable Cost of Screening Per Person Identified

- Testing for HBsAg in population with 2% chronic infection:

\$750 - \$3,752

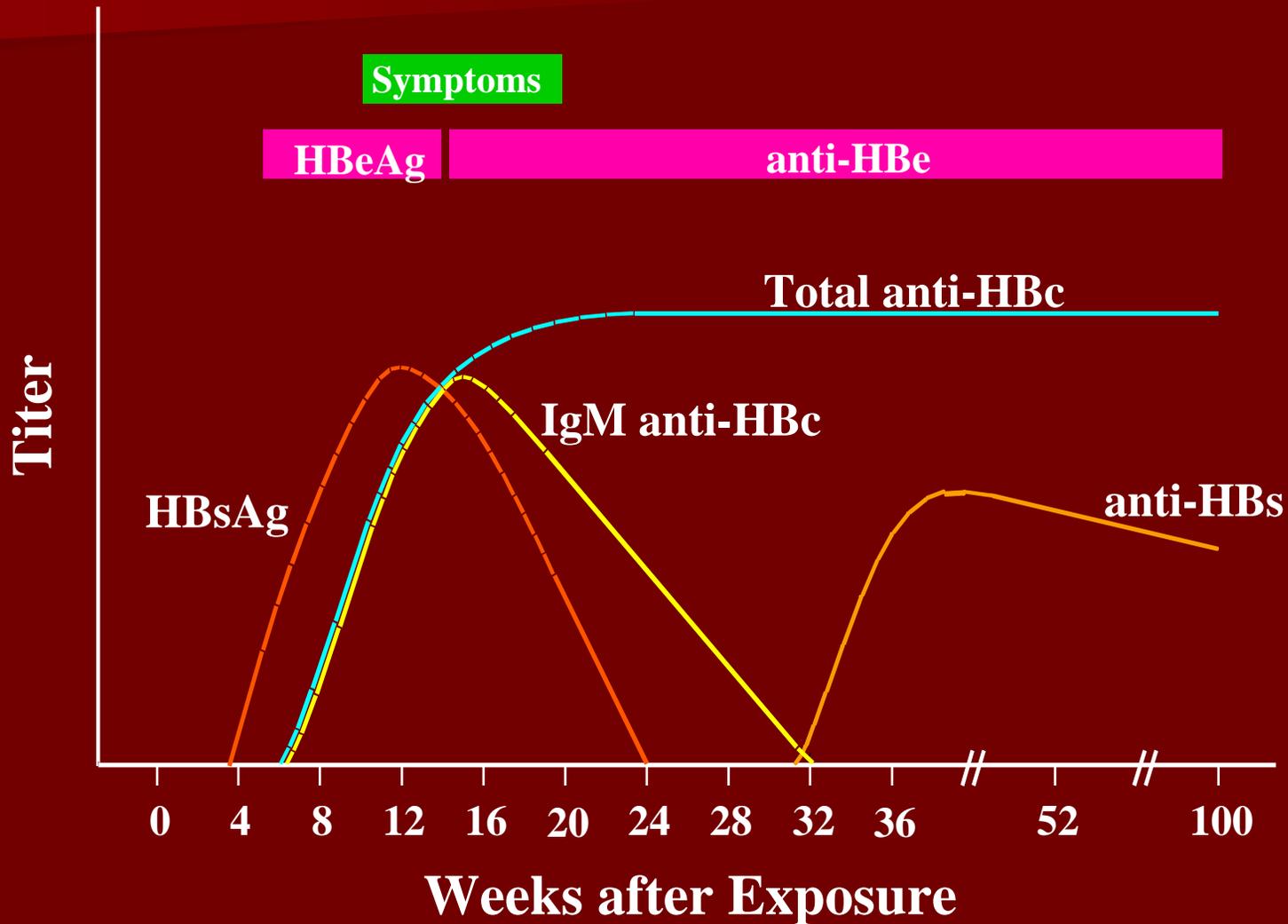
- Testing for HIV in a population with 1% infection prevalence:

\$1,733 - \$3,733

Antigen and Antibody Tests

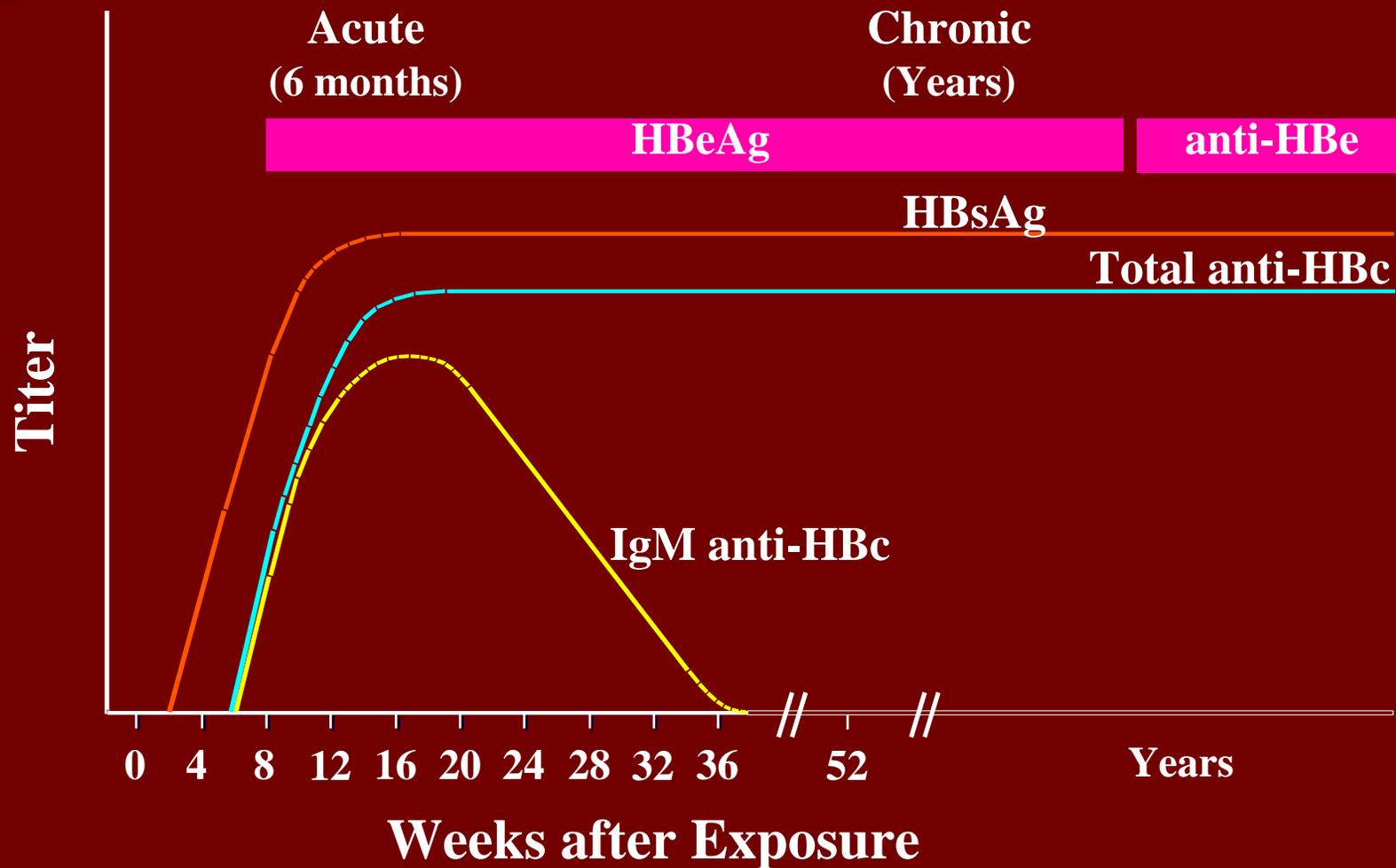
- Hepatitis B surface antigen (HBsAg) indicates presence of virus and that the person is infectious
- Hepatitis B e antigen (HBeAg) indicates viral replication
- Hepatitis B surface antibody (anti-HBs) indicates recovery and immunity
- Total Hepatitis B core antibody (anti-HBc) appears at onset and persists for life; indicates previous or ongoing infection
- IgM antibody to Hepatitis B core antigen (IgM anti-HBc) indicates recent infection, acute infection

Acute Hepatitis B Virus Infection with Recovery: Typical Serologic Course



Acute HBV Infection with Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course



Three Phases of Chronic Infection and Associated Lab Markers

Immune Tolerant – limited response from immune system

- High level of HBV DNA
- Hepatitis B e antigen positive (HBeAg)
- Absence of liver disease

Immune Active – immune system is active

- Positive or negative for Hepatitis B e antigen
- Positive for anti-body to HB e
- High levels of HBV DNA
- Active liver inflammation

Inactive Phase – asymptomatic, chronic

- Positive for antibody to HB e
- Normal liver aminotransferase levels
- Low or absent levels of HBV DNA

HBV Serology Interpretation

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
-	-	-	-	Never infected, no evidence of immunity
+	+	-	-	Chronic infection
+	+	+	-	Acute infection
-	+	-	+	Recovered from past infection, immune
-	-	-	+	Immune (natural or immunization)

Medical Benefit of Identification

- Allows for interventions that reduce morbidity and mortality including:
 - Clinical evaluation to monitor liver disease
 - Antiviral treatment which can delay or reverse liver disease
 - Baseline **alpha-fetoprotein (AFP)** measurement and ultrasound to detect Hepatocellular Carcinoma (HCC)
 - HAV vaccination
 - Counseling to reduce or eliminate alcohol use

Education for Patients with Chronic HBV infection

- Notify household, sexual and needle sharing contacts that they should be tested, vaccinated and if found susceptible, complete the series
- Practice safer sex until sex partners are vaccinated and their immunity documented
- Reduce other's exposure to your blood
 - Cover cuts, skin lesions; clean blood spills with bleach, don't share toothbrushes, razors
 - Don't donate blood, plasma, tissue, semen

Patient Education, con't

- Protect the liver from further harm:
 - Seek healthcare from a provider experienced in management of HBV
 - Avoid or limit alcohol consumption
 - Hepatitis A vaccination
- When seeking medical or dental care, patient should inform providers to promote appropriate evaluation and management
- Consider participating in a support group for people with chronic HBV

Patient Education, con't

- HBV is not spread by breastfeeding, kissing, hugging, coughing, sharing utensils or casual touching
- People with chronic HBV should not be excluded from school, play, child care, work or other settings unless they are prone to biting

Additional Education for Pregnant Women

- Pregnant women with chronic HBV infection should be counseled about the importance of:
 - Vaccination and HBIG for infant at birth
 - Completion of infant vaccination series
 - Post-vaccination testing to determine infection status or immunity

Additional Education for Health-care Workers

- Health-care workers living with chronic HBV infection should follow published guidelines and applicable state laws and regulations regarding recommended practices to reduce the risk of HBV transmission in the workplace

Partner Services

- Health care providers and public health staff should work together to promote notification of patient's sexual, needle sharing partners and household members
- Contacts should be tested, vaccinated and, if found susceptible, complete the series
- Well established partner services programs in STD/HIV programs may be able to provide guidance
- Partner services can play a critical role in reducing disease incidence

Medical Management of Persons with Chronic HCV Infection

- Evaluate soon after identification
- Consult with or refer to MD experienced in management of chronic liver disease
- Assess for:
 - risk of co-infection with HIV, HCV, HDV
 - history of alcohol use
 - family history of HBV and liver cancer

Medical Management of Persons with Chronic HCV Infection

- Lab testing:
 - Complete blood count (CBC), liver panel, markers of HBV replication, AFP, antibody for HAV, HIV and HCV
- Test persons from endemic areas for schistosomiasis
- Ultrasound for persons at risk of HCC
- Liver biopsy as per published guidelines

Treatment

- Seven therapies approved
 - Interferon alfa-2b
 - Peginterferon alfa-2a
 - Lamivudine
 - Adefovir dipivoxil
 - Entecavir
 - Telbivudine
 - Tenofovir disoproxil fumarate
- Two other antiviral medications are undergoing phase 3 trials for HBV treatment

Treatment

- Treatment decisions made on the basis of
 - HBeAg status
 - HBV DNA viral load
 - Alanine aminotransferase (ALT) a liver enzyme detected in the blood when the liver is damaged
 - Stage of liver disease
 - Age of patient
- Optimal duration of treatment not known
- More study of combination therapy needed

Serologic Endpoints of Therapy

- Loss of HBeAg
- HBeAg seroconversion in persons initially HBeAg positive
- Suppression of HBV DNA to undetectable levels in patients who are HBeAg negative and anti-HBe positive
- Loss of HBsAg

Additional Treatment Considerations

- For HBeAg positive patients, treatment should be continued for at least 6 months after loss of HBeAg and appearance of anti-HBe
- For HBeAg negative/ anti HBe positive patients, relapse rates are 80-90% if treatment is stopped in 1-2 years
- Viral resistance to lamivudine occurs in up to 70% of patients during the first 5 years

Implementation of These Recommendations

- Testing should be available in settings that serve populations included in the recommendations
 - Homeless shelters
 - STD treatment clinics
 - Refugee health clinics
 - Jails
 - TB clinics
 - Drug treatment
- Primary care settings
- OB/Gyn settings

Community Education and Outreach

- Collaboration is needed between public health, community organizations and community leaders to promote HBV testing and vaccination
- Address barriers to services in communities of color
- Community advisory groups can play a role in guiding these efforts

Resources

- To date, specific new funding has not been earmarked to implement these recommendations
- Additional resources are needed at the local, state and national level
- Additional providers with experience monitoring and treating patients with chronic HBV infection are needed

Educational Resources

- For more information about viral hepatitis
 - <http://www.cdc.gov/hepatitis/index.htm>
- Patient education resources for HBV
 - <http://www.cdc.gov/hepatitis/B/PatientEduB.htm>
- Provider education via on-line interactive case-based modules for clinicians
 - <http://depts.washington.edu/hepstudy/>
- NIH consensus conference on HBV management
 - <http://consensus.nih.gov/2008/2008HepatitisBCDC120main.htm>