



HIV MEDICAL ALERT

FOR PRIMARY HEALTH CARE PROVIDERS AND HEALTH PROFESSIONALS

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HIV Medical Alert

provides clinicians with comprehensive and up-to-date information about diagnosis, treatment, and prevention of HIV.

HIV Medical Alert

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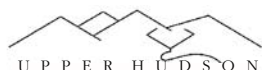
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WELCOME to the *HIV Medical Alert* Newsletter Continuing Medical Education (CME) format. This activity has been planned and implemented in accordance with the Essentials and Standards of the Medical Society of the State of New York through the joint sponsorship of Glens Falls Hospital and Upper Hudson Primary Care Consortium. The Glens Falls Hospital is accredited by the Medical Society of the State of New York (MSSNY) to sponsor continuing medical education for physicians.

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Hepatitis B in Primary Care, Part I

Hepatitis B virus (HBV) is recognized as a major disease and a serious global public health threat. Since the implementation of the world's first vaccine against Hepatitis B virus and changes in high-risk behaviors among populations at-risk for HIV/AIDS, the rate of infection has declined remarkably. However, even with these achievements, studies have shown that HIV-infected patients have higher rates of chronic HBV infection following exposure to HBV and often have increased frequency of hepatotoxicity with HIV drug therapy. Therefore among the core elements of HIV/AIDS care are HBV vaccination (if the patient is uninfected with HBV), monitoring of patients for Hepatitis B co-infection and subsequent HBV therapy for those who are infected with Hepatitis B virus.

The topic of Hepatitis B will be presented in a two-part series in *HIV Medical Alert*: Part I will discuss the principles of Hepatitis B in Primary Care; Part II (issued in December 2006) will describe the clinical treatment of the patient who is co-infected with HBV and HIV.

I. Hepatitis B Epidemiology

There are an estimated 60,000 new infections of Hepatitis B (HBV) in the United States each year. Approximately 80% of these new infections occur in adults and 8% among adolescents with the highest rate of disease occurring in 20-49 year olds. Hepatitis B is responsible for 3,000-5,000 deaths annually (CDC unpublished data, 2004).

Chronic Hepatitis B affects 1.25 million Americans. It is believed that 30% - 40% of these individuals likely acquired their infection in childhood before the implementation of the Hepatitis B vaccination programs.

Since the early 1990's the incidence of new HBV infections in children and adolescents has declined by 94%. This decline can be attributed to successful immunization programs to increase Hepatitis B vaccine coverage among children.

Globally, 2 billion people worldwide have been infected with Hepatitis B (1 out of 3 persons) and more than 1 million people in the world will die from complications due to Hepatitis B this year.

II. Prevention

The Hepatitis B vaccine is hailed as the first anti-cancer vaccine since it can protect against liver cancer by preventing Hepatitis B infection.

Hepatitis B vaccination coverage among adults at high risk, as measured by National Health Interview Survey (NHIS), has increased substantially from 30% in 2000 to 45% in 2004. Some of this increase in coverage represents the aging of persons vaccinated as adolescents, reflecting the effect of the Advisory Committee on Immunization Practices (ACIP) 1995 recommendations for routine vaccination of adolescents. In addition, higher vaccination coverage among persons of all ages at high risk likely contributed to a decline in Hepatitis B incidence. From 2000 to 2004, Hepatitis B incidence among adults decreased 27%, from 3.7 to 2.7 per 100,000 population (CDC, unpublished data, 2006). However, Hepatitis B vaccination coverage of adults at high risk remained lower than vaccination coverage of children (92%) and adolescents (86%) in 2004, which are two other age groups included in ACIP vaccination strategy to eliminate HBV transmission.

(MMWR, May 12, 2006/ 55[18];509-511)

Recommendations of the ACIP, Part I: Immunization of Infants, Children, and Adolescents

- Universal vaccination of infants beginning at birth
- Prevention of perinatal HBV infection through
 - Screening all pregnant women for Hepatitis B surface antigen (HBsAg)
 - Immunizing infants born to HBsAg-positive mothers and infants born to women with unknown HBsAg status
- Routine vaccination of all previously unvaccinated children and adolescents
- Vaccination of previously unvaccinated adults at increased risk for infection

(MMWR, December 23, 2005/54(RR16); 1-23)

The second part of these recommendations, which will include updated recommendations and strategies to increase vaccination of adults will be published at a later date. In the meantime, the Advisory Committee on Immunization Practices (ACIP) has published provisional recommendations for adult vaccination in October 2005.

Provisional Recommendations for Hepatitis B Vaccination of Adults:

- Hepatitis B vaccination is recommended for all unvaccinated adults at risk for Hepatitis B virus (HBV) infection and for all adults seeking protection from HBV infection. Acknowledgement of a specific risk factor is not a requirement for vaccination.
- In settings where a high proportion of adults are likely to have risk factors for HBV infection all unvaccinated adults should be assumed to be at risk and should receive Hepatitis B vaccination. These settings include:
 - Sexually Transmitted Disease treatment facilities,
 - HIV testing facilities,
 - HIV treatment facilities,
 - Substance Abuse treatment and prevention facilities
 - Correctional facilities,
 - Health care settings serving men who have sex with men,
 - Chronic hemodialysis facilities and end-stage renal disease programs, and
 - Institutions and nonresidential daycare facilities serving developmentally disabled persons.
- Standing orders should be implemented to identify and vaccinate eligible adults in primary care and specialty medical settings. If determining risk for HBV infection is a barrier to vaccination in these settings, providers may use alternative vaccination strategies such as offering Hepatitis B vaccine to all unvaccinated adults in age groups with highest risk of infection (e.g., < 45 years)

For further information on recommended doses and schedules of Hepatitis B vaccine go to: <http://www.immunize.org/catg.d/2081ab.htm>

Booster doses

Current data show that vaccine –induced Hepatitis B surface antibody (anti-HBs) levels may decline over time; however, immune memory (anamnestic anti-HBs response) remains intact indefinitely following immunization. Persons with declining antibody levels are still protected against clinical illness and chronic disease. For health care workers with normal immune status who have demonstrated an anti-HBs response following vaccination, booster doses of vaccine and periodic anti-HBs testing are not recommended. (cdc.gov/hepatitis – fact sheet)

Post-vaccination Testing

After routine vaccination of infants, children, adolescents or adults post-vaccination testing for adequate antibody response is not necessary. Post-vaccination testing IS recommended for persons whose medical management will depend on knowledge of their immune status.

This includes persons who:

- Are immunocompromised (e.g. hemodialysis patients)
- Received the vaccine in the buttock
- Are infants born to HBsAg –positive mothers
- Are healthcare workers who have contact with blood
- Are sex partners of persons with chronic Hepatitis B infection

Post-vaccination testing should be completed 1-2 months after the third vaccine dose for reliable results. A protective antibody response is >10mIu/ml.

Fiscal constraints are a significant barrier to providing adult Hepatitis B vaccination. Though Medicare covers Hepatitis B vaccine administration for persons at intermediate or high risk for Hepatitis B, there is no federal policy for Medicaid reimbursement for vaccination. Private insurance plans and health maintenance organizations generally operate independently in determining reimbursable services and reimbursement varies with each plan.

(CDC.gov – Hepatitis: Partners Meeting)

Hepatitis B: Are your patients at risk?

Do you have patients:

- who are adolescent?
- who are sexually active with multiple partners?
- living with people who are chronic carriers of Hepatitis B virus?
- whose jobs potentially expose them to human blood or body fluids?
- who use illicit drugs?
- who travel internationally to endemic areas?
- who were born in Asia, Africa, the Amazon Basin in South America, the Pacific Islands, Eastern Europe, or the Middle East?
- who are Native Americans or Alaskan Natives?
- who have hemophilia?
- who are receiving hemodialysis treatment?
- who are monogamous but whose partners are at risk for Hepatitis B virus infection?

If you responded yes to any one of these questions, you have patients who are at risk of infection with the Hepatitis B virus.

(National Foundation for Infectious Diseases)

Table A	
RISK FACTORS	
Heterosexual transmission	39%
MSM.....	26%
IDU	17%
None identified	14%
Other, household contact, occupational exposure, hemodialysis, institutional, transfusion	4%

Table B	
TRANSMISSIONS	
• Unprotected sex	
• Sharing IV drug needles	
• Living in a household with an infected person	
• An infected mother to her newborn child at birth	
• Sharing earrings, razors or toothbrushes with an infected person	
• Unsterilized needles, including tattoo or piercing needles	
• Human bites	

III. Screening – Hepatitis B

When screening for Hepatitis B the initial testing includes a Hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (anti-HBs) and a Hepatitis B core antibody (anti-HBc).

Table 1, published by the CDC, helps clinicians in interpreting these test results.

The presence of a confirmed HBsAg result is indicative of ongoing HBV infection. All HBsAg-positive persons should be considered infectious. In newly infected persons, HBsAg is the only serologic marker detected during the first 3-5 weeks after infection, and it persists for variable periods at very low levels. The average time from exposure to detection of HBsAg is 30 days (range: 6-60 days). Highly sensitive single-sample nucleic acid tests can detect HBV DNA in the serum of an infected person 10-20 days before detection of HBsAg. Transient HBsAg positivity has been reported for up to 18 days after vaccination and is clinically insignificant.

Anti-HBc appears at the onset of symptoms or liver test abnormalities in acute HBV infection and persists for life. Acute or recently acquired infection can be distinguished by the presence of the IgM class of anti-HBc, which is detected at the onset of acute Hepatitis B and persists for up to 6 months if the disease resolves.

In persons who recover from HBV infection, HBsAg is eliminated from the blood, usually within 3-4 months, and anti-HBs develops during convalescence. The presence of anti-HBs typically indicates immunity from HBV infection. In persons who become chronically infected, HBsAg and anti-HBc persist, usually for life.

HBsAg (Hepatitis B e antigen) can be detected in the serum of persons with acute or chronic HBV infection. The presence of HBsAg correlates with viral replication and high levels of virus. (i.e. high infectivity)

Persons who are surface antigen and core antibody positive are chronically infected and additional testing is indicated. Hepatitis B “e” antigen and “e” antibody and a Hepatitis B DNA are the tests that should be done.

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The presence of a positive HBV DNA in the presence or absence of the “e” antigen indicates viral replication. A positive HBV DNA and a negative “e” antigen indicate that the patient has a precore mutant of

Table 1
Typical interpretation of serologic test results for Hepatitis B virus infection

HbsAg*	Serologic marker			Interpretation
	Total anti-HBc†	IgM [§] anti-HBc	Anti-HBs¶	
—**	—	—	—	Never infected
††§§	—	—	—	Early acute infection; transient (up to 18 days) after vaccination
+	+	+	—	Acute infection
—	+	+	—	Acute resolving infection
—	+	—	+	Recovered from past infection and immune
+	+	—	—	Chronic infection
—	+	—	—	False positive (i.e., susceptible); past infection; "Low-level" chronic infection;¶¶ passive transfer to infant born to HBsAg-positive mother
—	—	—	+	Immune if concentration is ≥10mIU/mL,***passive transfer after Hepatitis B immune globulin administration

* Hepatitis B surface antigen.
† Antibody to Hepatitis B core antigen.
§ Immunoglobulin M.
¶ Antibody to HBsAg.
** Negative test result
†† Positive test result
§§ To ensure that an HBsAg-positive test result is not a false positive, samples with repeatedly reactive HBsAg results should be tested with a licensed (and, if appropriate, neutralizing confirmatory) text.
¶¶ Persons positive for only anti-HBc are unlikely to be infectious except under circumstances in which they are the source for direct percutaneous exposure of susceptible recipients to large quantities of virus (e.g., blood transfusion or organ transplant).
*** Milli-International Units per milliliter.

Hepatitis B. Both of these situations warrant further evaluation with a liver biopsy and possible treatment. A positive Hepatitis B surface antigen with a negative HBV DNA and a negative “e” antigen suggest that the patient is a carrier of Hepatitis B and in a non-replicative state. (MMWR – December 23, 2005)

Screening – Liver Functions Tests

Abnormal lab values may surface in screening test panels which now routinely include liver function tests such as ALT (alanine aminotransferase), AST(aspartate aminotransferase), serum albumin concentration, prothrombin time, and serum bilirubin. The primary care provider will then conduct a complete medical history which is the single most important part of the evaluation of the patient with elevated LFT’s. The physical examination should focus upon findings that suggest the presence of liver disease. Laboratory testing is a critical step in guiding the evaluation. There is no consensus on the cost-effective approach to the evaluation of patients with abnormal LFT’s.

For a complete review of how to assess a patient with abnormal liver function tests go to www.cdc.gov/ncidod/diseases/hepatitis/b/hbv_silent_killer.pdf

IV. Acute Hepatitis B

The onset of acute disease is usually insidious. Infants and young children (aged <10 years) are typically asymptomatic. When present, clinical symptoms and signs might include anorexia, malaise, nausea, vomiting, abdominal pain, and jaundice. Extra hepatic manifestations of disease (e.g. skin rashes, arthralgias, and arthritis) also can occur. The fatality rate among persons with reported acute Hepatitis B is 0.5% - 1.5%, with highest rates in adults age > 60 years. (CDC)

No specific treatment exists for acute Hepatitis B. (CDC) About 90% of people who experience acute Hepatitis B infection will develop an effective immune response and will not develop chronic infection.

V. Chronic Hepatitis B

Approximately 5-10% of adults, 30-50% of children and 90% of babies who are infected with HBV will develop chronic infection. Persons with chronic HBV serve as the major reservoir for continued HBV transmission.

Twenty-five percent of people with chronic infection will go on to develop liver disease, including liver cancer, cirrhosis or liver failure.

Chronic Hepatitis B causes 80% of primary liver cancer worldwide. Liver cancer is the 3rd leading cause of death in the world. In the US, liver cancer rates are increasing as most other types of cancer are decreasing

Persons with chronic Hepatitis B infection require medical evaluation and regular monitoring to determine if and when intervention with antiviral therapy is needed and to observe for serious sequelae (AASLD practice guidelines). Treatment for HBV can achieve sustained suppression of HBV replication and remission of liver disease in certain persons.

These additional guidelines also offer recommendations for the treatment of chronic Hepatitis B., who to treat and what treatment to use.

Recommendations for monitoring patients with chronic HB infection

1. HBeAG-positive patients with elevated ALT levels and compensated liver disease should be observed for 3-6 months for spontaneous seroconversion from HBeAG to HBe antibody prior to initiation of treatment
2. Patients who meet the criteria for chronic Hepatitis B (serum HBV DNA >105 copies/mL and persistent or intermittent elevation in aminotransferase levels) should be evaluated further with a liver biopsy
3. Patients in the inactive Hepatitis B surface antigen (HBsAg) carrier state should be monitored with periodic liver chemistries every 6-12 months, as liver disease may become active even after many years of quiescence.

(“Chronic Hepatitis B: Update on Recommendations” The American Association for the Study of Liver Diseases, September 2003, www.aasld.org)

VI. Challenges for the Coming Years

The national health objectives for 2010 call for a 75% - 90% reduction of acute Hepatitis B cases among high-risk adults. Primary care providers can effectively advance this objective by conducting risk-assessments, delivering persuasive prevention messages and sustaining high Hepatitis B vaccine coverage rates. Complete elimination of HBV transmission is achievable, but only with expanded efforts to vaccinate adults who are at increased risk for HBV infection. Primary care sites provide a sound and feasible setting for effective HBV prevention.

Part II - HBV and HIV Co-Infection – December 2006 Issue

Author

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Continuing Education Test

HIV Medical Alert September 2006 Vol. 10 Issue No. 2: Hepatitis B in Primary Care, Part I

To earn credit:

1. Read the CME article.
2. Review the objectives
3. Study and apply the content to the objectives and to your practice.
4. Complete the Post-Test.
5. **Return the answer sheet as directed at the bottom of the evaluation page.**

Objectives: At the conclusion of this activity, the learner will be able to:

1. Discuss the Provisional Recommendations for Hepatitis B Vaccination of Adults.
2. Name a resource for schedules of Hepatitis B vaccination and recommended doses.
3. List 5 situations in which post-vaccination testing is recommended.
4. State the importance of regular monitoring and medical evaluation of a person with chronic Hepatitis B.

Note: This CME activity and quiz is designated for 1 credit. CME credit expires September 5, 2008

Select the best answer for each of the following.

1. Settings in which adults should be considered at risk and receive Hepatitis B vaccination are:
 - a. Sexually Transmitted Disease clinics
 - b. HIV testing and treatment facilities
 - c. Correctional Facilities
 - d. Drug abuse treatment and prevention facilities
 - e. All of the above
2. Post Vaccination Testing should occur in all of the following persons EXCEPT:
 - a. Immunocompromised
 - b. Sex partners of persons with chronic Hepatitis B
 - c. Vaccine received in buttock
 - d. All adolescents
3. The website where further information may be obtained regarding Hepatitis B schedules and doses is:
 - a. www.hivguidelines.org
 - b. www.immunize.org/catg.d/2081ab.htm
 - c. www.anacnet.org
 - d. www.cdc.gov
4. If a person has a chronic Hepatitis B infection you would expect the following lab results:
 - a. Positive HBsAg, negative total anti-HBc, negative IgM anti-HBc, negative Anti-HBs
 - b. Positive HBsAg, negative total anti-HBc, negative IgM anti-HBc, negative Anti-HBs
 - c. Negative HBsAg, Positive total anti-HBc, negative IgM anti-HBc, negative Anti-HBs
 - d. Positive HBsAg, Positive total anti-HBc, negative IgM anti-HBc, negative Anti-HBs
5. Persons with chronic Hepatitis B infection require medical evaluation and regular monitoring to determine if and when intervention with antiviral therapy is needed and to observe for serious sequelae.
 - a. True
 - b. False

Evaluation of CME Activity

HIV Medical Alert September 2006 Vol. 10 Issue No. 2: Hepatitis B in Primary Care, Part I

	Excellent	Good	Fair	Needs Improvement
Overall Activity				
1. Was the subject matter well balanced in fact and theory?	1	2	3	4
2. Was the format clear and easy to read?	1	2	3	4
3. Did subject matter have sufficient detail?	1	2	3	4
4. Was subject matter valuable for practical application?	1	2	3	4
5. Were objectives listed on test page met?	1	2	3	4
6. Was the writer clear in content, sequence and style?	1	2	3	4
7. Overall program was? _____				

Comments/Topic Suggestions:

PLEASE PRINT CLEARLY TO ASSURE ACCURATE DOCUMENTATION OF CME CREDIT

Profession: Physician PA NP CNM RN LPN Other _____

Name: _____ **County:** _____

Organization: _____

Address: _____
Street City/Town State/Zip

Signature: _____

(please sign legibly for CME records)

Return the completed test and evaluation form to:

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