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ABOUT IDCR

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AN APPROACH TO HEPATITIS B VIRUS IN THE CORRECTIONAL SETTING

- **Spotlight:**
  The 2008 Conference on Retroviruses And Opportunistic Infections (CROI)
- **HBV 101:**
  FDA Approved Medications For Prevention And Treatment Of Hepatitis B Virus

OBJECTIVES

- The learner will be able to describe the recommended treatment, dosing, and monitoring options for the treatment and management of the hepatitis B virus.
- The learner will be able to explain the prevention, screening, and diagnosis measures for the hepatitis B virus.
- The learner will be able to discuss the most significant studies presented at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI).

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Purpose Statement

The purpose of this monograph is to increase the knowledge of physicians in correctional systems in the prevention, diagnosis, treatment, and management options for hepatitis B and become familar with the information presented at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI).

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An Approach To Hepatitis B Virus In The Correctional Setting

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Introduction

Approximately 1.25 million persons in the United States are chronically infected with hepatitis B virus (HBV).[1,2] An estimated 2% of inmates in the U.S. have chronic HBV infection, five times the prevalence found in non-incarcerated populations.[3] Almost one third of new HBV cases in the U.S. each year occur among inmates or those who have been incarcerated.[4] Although most HBV-infected inmates acquired the infection prior to incarceration, transmission of HBV has been well documented within jails and prisons.[5] This article will review basic concepts of HBV transmission, prevention, diagnosis, and treatment including special considerations for the management of hepatitis B in correctional settings.

Transmission

HBV is transmitted percutaneously and by mucosal contact with the blood and body fluids of chronically infected persons. In the United States, most new cases of HBV are due to sexual activity or injection drug use among unvaccinated adults. Less commonly, HBV is transmitted through occupational and health care associated mucosal or percutaneous exposure to blood. Outbreaks of HBV have been linked to contaminated equipment used for injections and acupuncture.[6, 7]

Other recognized risks for HBV infection include sharing a toothbrush, razor, or other device that has come into contact with blood from a person who is chronically infected with HBV. Although skin or mucosal contact with saliva from an HBV infected person has not been linked to transmission of the virus, transmission has occurred through a human bite.[8]

Natural history of HBV infection

Acute HBV infection is usually asymptomatic. Those who do become clinically ill may experience an insidious onset of nausea, emesis, abdominal discomfort, and anorexia. Arthralgias, rash, and icterus may develop. Primary infection is generally self limited, does not lead to chronic viremia, and results in long term immunity to re-infection. The likelihood that chronic HBV will develop depends upon the age at acquisition and the immune status of the person who becomes infected. Approximately 5% of HIV negative adolescents and adults who become infected with HBV will develop chronic infection, and 15-25% of those who are chronically infected will develop cirrhosis, liver cancer, or liver failure due to HBV.[9,10] HIV/HBV co-infection is associated with decreased clearance of hepatitis B surface antigen and e antigen and increased HBV viremia.[11] Co-infection with HIV and HBV is also associated with increased mortality as compared to HIV monoinfection.[12] Untreated infants who acquire HBV perinatally have a 90% risk of chronic infection.[13]

Prevention

Routine immunization of infants, children, and adolescents has contributed to a dramatic decline in the incidence of new cases of HBV, and continued effort to achieve universal childhood HBV vaccination is the best strategy for HBV elimination. Currently, most acute cases of HBV develop among unvaccinated adults. Although most adults will accept HBV vaccination if it is offered to them, many at-risk adults who are at highest risk for acute HBV infection do not have ready access to free or low cost vaccination services.[14] Correctional facilities can be ideal settings in which to reach adults who are at-risk for HBV infection.

The Advisory Committee on Immunization Practices (ACIP) recommends that HBV vaccination be provided to all non-immune inmates of correctional facilities. Routine vaccination can be facilitated through the use of standing orders for screening and immunization.[15] HBV vaccination consists of 3 intramuscular doses in the deltoid muscle administered by one of the following schedules: 0, 1, and 6 months; 0, 1, and 4 months; 0, 2, and 4 months, or 0, 1, 2, and 12 months. A combined hepatitis A virus (HAV) and HBV vaccine (Twinrix) is also available for adults who are non-immune to both viruses. Twinrix can be administered at either 0, 1, and 6 months; or an accelerated schedule of 0, 7, and 21-30 days, followed by a dose at 12 months. The latter schedule is particularly useful in jails and other short-stay situations. (See **Table 1** for additional dosing information).

The percentage of those who will develop a protective level of HBV antibodies is decreased in hemodialysis patients, HIV infected persons, men, those > 50 years old, and smokers.[16] Using a double dose of vaccine has been shown to improve the response rate to immunization in dialysis patients and those who are HIV infected.[17]

In general, it is not necessary to test for immunity following HBV vaccine. Testing should be considered for those who will be at high risk for ongoing exposure to blood or body fluids. Those who failed to develop a protective level of HBsAb should receive another course of three doses of vaccine. Revaccination leads to protective antibody levels in 50-100% of recipients.[18] Persons with chronic HBV should not donate organs, blood, or semen.

Post Exposure Prophylaxis (PEP) for HBV

Pregnant women should be screened for HBV so that prophylaxis can be given to the newborns of those with chronic HBV infection. Administration of one dose of hepatitis B immune globulin and initiating the three dose HBV vaccination series within 24 hours after birth is 85%-95% effective in preventing both HBV infection and the chronic carrier state.[13]

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Letter from the Editor

Dear Correctional Colleagues,

This week, the Pew Center on the States announced that an all-time high of more than one in 100 adult Americans are currently in jail or prison. In addition, the Center reported that more than $49 billion was spent on corrections last year, more than four times as much as twenty years ago. The U.S. continues to lead all other countries in both the number and percentage of incarcerated citizens.

Those of us who work in correctional public health certainly have little impact upon how many individuals this country chooses to incarcerate. We can, however, make an enormous difference in the health of this nation by ensuring that inmates who are entrusted to our care benefit from our best efforts at education, prevention, diagnosis, and treatment.

One area in which we can make a significant impact is chronic viral hepatitis. Hepatitis B virus (HBV) immunization efforts targeting infants, children, and adolescents have achieved significant success in the U.S. over the past two decades. As a result, non-immune adults now account for the overwhelming majority of new HBV infections in this country. In most jails and prisons the prevalence of HBV is markedly higher than that seen in the general U.S. population, and nearly 30% of persons with acute HBV have been incarcerated. Approximately 5% of adults who become infected with HBV will develop chronic hepatitis. Persons with chronic viral hepatitis are at risk for developing cirrhosis, end stage liver disease, and hepatocellular carcinoma.

Inmates continue to engage in behaviors that place them at risk for viral hepatitis both while incarcerated and after being released to the community. As a result, non-immune inmates comprise a group who would potentially benefit from hepatitis prevention initiatives. It has become increasingly clear that any effective comprehensive national strategy for the prevention, early diagnosis, and treatment of viral hepatitis must include jails and prisons.

The Advisory Committee on Immunization Practices (ACIP) has called for routine vaccination of all inmates who are not known to be immune regardless of their length of stay. Immunization of non-immune adults, diagnosis and treatment of those who are chronically infected, substance abuse treatment, and harm reduction education in the correctional setting can benefit our patients and the free community by reducing transmission and by decreasing costs associated with chronic viral hepatitis.

This month, Dr. Jennifer Cocohoba presents a comprehensive update regarding HBV. Dr. Cocohoba addresses the ongoing evolution of HBV treatment, including the particular challenges of treating those who are co-infected with HIV. Morris Jackson reviews some of the most useful information from last month's Conference on Retroviruses and Opportunistic Infections (CROI), and the IDCR News and Reviews provides additional data from CROI 2008.

As always, we at IDCR thank you for your continued readership. We also encourage you to communicate with us regarding infectious diseases topics that you would like to see addressed in future issues.

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HBV PEP should be initiated for any non-immune person who has occupational percutaneous or mucosal exposure to blood from a chronically infected individual.[13,19]
(See **Table 2**)

Screening and diagnosis

The American Association for the Study of Liver Diseases recommends HBV screening for all inmates of correctional facilities.[20] If screening is conducted solely to identify those who are unlikely to benefit from immunization, testing for anti-HBc (HBcAb) and anti-HBsAg (HBsAb) will identify those who have previously been infected or immunized. If the goal is to identify both those who are immune and those who have chronic HBV, it may be more useful to obtain both HBsAg and anti-HBsAg (HBsAb). **Table 3** describes the interpretation of HBV serologic markers.

Vaccinating those who are already immune to HBV because of prior immunization or infection does not cause adverse effects. Whether or not screening should be conducted prior to vaccination depends upon the baseline prevalence of immunity and chronic HBV infection in the population being immunized. In a study conducted in the Texas Department of Corrections, the cost of prevaccination testing was equivalent to that of vaccination without testing when the underlying HBV prevalence reached 25%.[21]

Diagnosis of chronic HBV infection

Chronic HBV infection should be considered in those who have persistent elevations in liver transaminases. The diagnosis can be confirmed by the presence of hepatitis B surface antigen that persists for greater than 6 months. Occasionally, the only HBV serologic marker that is present is anti-HBc. Isolated anti-HBc can be a false positive, can be found in those who have recovered from HBV infection but have waning levels of HBsAb, who are chronically infected and have low levels of HBsAg.

The initial evaluation of a patient who has chronic HBV should include a complete history and physical examination. Blood testing should include a complete blood count with platelets, transaminases, albumin, prothrombin time, and serologies for hepatitis A, C, delta, and HIV. Hepatitis B specific laboratory tests include hepatitis B surface antigen, e antigen, anti-HBe, and hepatitis B viral DNA. A serum alpha fetoprotein and ultrasound or CT should be obtained every 6-12 months to screen for hepatocellular carcinoma. Liver biopsy is not routinely necessary in the diagnosis and management of chronic HBV.[20]

Treatment of HBV

Goals of therapy

The goals of HBV treatment are to suppress viral replication, seroconvert from HBsAg to HBsAb and HBeAg to HBeAb, and prevent long-term liver damage that can result in cirrhosis, liver failure, and hepatocellular carcinoma. Treatment is generally recommended for chronically infected patients who are HBeAg(+) with ALT levels persistently greater than 2 times upper limit of normal, and for patients who are HBeAg(-) with HBV DNA greater than 20,000 IU/mL and ALT levels persistently greater than 2 times upper limit of normal.[20] Treatment should be considered for patients who are HBeAg(+) with ALT levels 1-2 times the upper limit of normal and those who are HBeAg(-) with HBV DNA levels between 2,000 and 20,000 IU/mL and ALT 1-2 times upper limit of normal.[20]

Available treatments (See HBV 101)

Interferons
Interferon alfa was the first FDA approved agent for the treatment of hepatitis B. In clinical trials, therapy with interferon resulted in 32-79% of participants clearing HBV-DNA, but only 10-15% demonstrated seroreversion of the HBsAg.[22-26] Predictors of a favorable response to interferon therapy include lower baseline levels of HBV DNA and high aminotransferase levels. Due to the inconvenience of multiple weekly subcutaneous injections, treatment with interferon has largely been replaced by once weekly pegylated interferon and oral nucleoside/nucleotide analogs.
Seroconversion of HBeAg and HBsAg is more frequent with peg-interferon compared to lamivudine over shorter study periods. However, treatment with lamivudine is not usually given short term.[27,28]

Nucleoside and Nucleotide analogs
Nucleoside and nucleotide analogs interfere with the ability of the HBV polymerase to synthesize viral DNA. With all agents in this class, there is a risk of acute HBV exacerbation upon abrupt cessation of therapy. In clinical trials, most cases were marked by asymptomatic increases in liver transaminases and increases in HBV viremia, although a few cases were fatal. Care must be taken to taper, substitute, or monitor closely when these HBV therapies are discontinued.

Lamivudine (Epivir HB)
Lamivudine was the first oral medication approved by the FDA for the treatment of HBV, and is generally well-tolerated A study of 651 Chinese patients randomly assigned to receive lamivudine or placebo was terminated after a median of 32.4 months due to a difference in hepatic disease progression and death between the treatment and placebo arms (7.8% versus 17.7%, HR for progression =0.45, p =0.001).[29] In an Italian study, 93.9% of HBeAg(-) patients achieved a HBV virological response after approximately 22 months treatment. At the 4-year follow up, the proportion with a virologic response had decreased to 39%. In the multivariable analyses, viral breakthrough increased the risk for hepatocellular carcinoma and end stage liver disease. (p< 0.001).[30] In another double-blind placebo controlled clinical trial of 139 HBeAg(-) patients, a median 3.21 log copies/mL reduction in HBV DNA was achieved in the lamivudine arm compared to only 0.47 log copies/mL (p < 0.001) for placebo. After 244 months, more lamivudine patients (56% vs. 11%, p < 0.001) had achieved a complete response to therapy.[31] In a smaller study of 34 HBeAg(+) patients treated with lamivudine for one year, 70.6% at one year, 64.7% at 2 years, and 55.8% at 3 years had undetectable HBV DNA and normalization of transaminase levels.[32] Another small study of 20 Japanese patients treated with lamivudine for more than one year, and followed for a median of 8.5 years, found a 30% increase in HBeAg clearance and a 55% increase in the proportion of patients with undetectable HBV DNA at the end of the study.[33]

The efficacy of lamivudine does not appear to be affected by renal transplant or hemodialysis.[34] Resistance to lamivudine is conferred by a mutation in the YMDD region of the HBV polymerase. This mutation is common and occurs in 24%, 56%, and 75% of patients after one, two, and three years respectively. A small study in 30 patients suggests that early detection of the YMDD mutation may be useful for predicting virologic breakthrough at 24 months (p=0.003).[35] Clinical benefits to lamivudine therapy may be decreased in patients who develop the YMDD mutation. In a study of 74 patients who continued on lamivudine therapy for 3 years, 15% versus 64% demonstrated histologic improvement at 3 years, 54% versus 32% remained unchanged, and 31% versus 5% worsened histologically for those with the YMDD versus wild-type variant.[36]

Adefovir (Hepsera)
Adefovir was initially evaluated for its anti-HIV activity before dose-limiting renal toxicity halted further study. It was later discovered that adefovir completely inhibits HBV viral replication at lower, less nephrotoxic doses. One large clinical trial of adefovir in 185 HBeAg(-) patients randomly assigned participants to receive treatment or placebo for 48 weeks.[37] At 48 weeks, participants were again randomly assigned to receive adefovir versus placebo for an additional 48 weeks of therapy. Median HBV DNA reduction among those receiving adefovir was 3.63 log copies/mL, and 79% of participants had an undetectable HBV DNA at 144 weeks.

Potential adefovir resistance mutations were identified in 5.9% of patients after 144 weeks of therapy. 125 subjects enrolled in a continuation arm of this study to 240 weeks demonstrated a durable response. In 67% of participants HBV DNA remained < 1000 copies/mL, ALT levels remained normalized in 69%, and 73% had decreased fibrosis.[38] A randomized clinical trial of adefovir versus placebo in 515 HBeAg(+) patients found 53% versus 25% histologic improvement (p < 0.001), 21% versus 0% undetectable HBV-DNA (p<0.001), and 48% versus 16% ALT normalization (p<0.001) at 48 weeks.[39] In addition, HBeAg seroconversion was achieved in 12% versus 6% of patients (p=0.049). A randomized double-blind placebo-controlled clinical trial of adefovir in 480 Chinese subjects found a median reduction of 4.5 log copies/mL, 28% of subjects undetectable HBV DNA, and 79% of subjects with normalization of ALT at 52 weeks.[40]

Adefovir is active versus lamivudine-resistant HBV and may be useful for salvage therapy. A number of studies have looked at the combination of lamivudine and adefovir for the treatment of lamivudine resistant HBV, however the clinical and serologic benefits of combination therapy are not yet well-established.[41-47] There is insufficient data to recommend combination therapy in treatment naive individuals. Adefovir is effective in patients with renal insufficiency, those undergoing hemodialysis, and those who have had a kidney transplant.[48, 49]

Entecavir (Baraclude)
Entecavir is a potent guanosine nucleoside analogue for the treatment of HBV. In a phase 3 double blind randomized study of entecavir versus lamivudine in 648 HBeAg(-) patients, a higher proportion of entecavir treated subjects demonstrated histologic improvement (70% versus 61%, p=0.001), undetectable HBV DNA (90% vs 72%, p < 0.001) and normalization of ALT levels (78% vs. 71%, p=0.045) at 48 weeks.[50] A phase 3 trial of entecavir versus lamivudine in 715 HBeAg(+) patients also found a higher proportion of histologic improvement (72% vs 62%, p =0.009), undetectable HBV DNA (67% vs. 36%, p < 0.001) and normalization of ALT (68% vs. 60%, p =0.02) for entecavir treated subjects.[51] These outcomes appear to be similar after 2 years of therapy: in a study of 709 HBeAg(+) patients 80% vs 39% (p< 0.0001) achieved undetectable HBV DNA and 87% vs 79% (p =

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0.0056) demonstrated normalization of ALT levels at 96 weeks, though there was no difference in HBeAg seroconversion (31% vs. 25%).[52] The incidence of resistance to entecavir is thought to be low and develops via a two-step process which requires lamivudine resistance mutations to develop in combination with further mutations. Therefore, although entecavir appears to be effective in the treatment of lamivudine-resistant HBV, it is not recommended to use them in combination.[53-55]
In comparison to adefovir, entecavir has been shown to be superior for virological endpoints in both HBeAg(-) and HBeAg(+) populations and for ALT normalization and seroconversion in HBeAg(+) individuals. Entecavir was also superior to adefovir for histological endpoints in HBeAg(+) persons, and comparable in HbeAg(-) persons.[56]

Telbivudine (Tyzeka)
Telbivudine is the newest nucleoside analogue approved for the treatment of hepatitis B. In a 1370 person, randomized, non-inferiority trial of telbivudine 600mg versus lamivudine 100mg, telbivudine was non-inferior to lamivudine for HBeAg(-) patients in achieving normalization of ALT or a histologic response after 52 weeks of therapy.[57] For HBeAg(+) patients, a higher proportion achieved a histologic response in the telbivudine arm (64.7% vs 56.3%, p =0.01) compared to lamivudine arm. Telbivudine has also been compared to adefovir in a 52-week open label study of 135 HBeAg(+) patients.[58] Subjects received telbivudine for 52 weeks, adefovir for 52 weeks, or adefovir for 24 weeks, followed by telbivudine for 28 weeks. At week 24, patients in the telbivudine arm had a higher odds of having undetectable HBV DNA compared to the other arms pooled together (OR 4.46 1.86-10.72, p=0.001). There do not appear to be significant drug-drug interactions between telbivudine and adefovir or lamivudine.[59] Single dose studies have suggested that telbivudine can be used across varying degrees of hepatic impairment and that its pharmacokinetics are unaltered if co-administered with food.[60,61] Telbivudine also selects for mutations in the YMDD region of HBV polymerase though at a slower rate than lamivudine (4.4% after 1 year, 21.6% after 2 years). Adefovir may also be useful for patients who have developed resistance to telbivudine.

Combination Interferon/nucleoside therapy
In a randomized, controlled, open-label trial of 100 HBeAg-positive patients, sustained seroconversion and HBV DNA < 500,000 copies was achieved in a higher proportion of patients treated with peg-interferon plus lamivudine (36%) versus lamivudine alone (14%).[27] In a study of 814 HBeAg-positive patients more subjects assigned to peg-interferon plus lamivuine or peg-interferon alone achieved HBeAg seroconversion (32% vs. 27% vs. 19 %; p = 0.02 and p < 0.001 respectively) compared to treatment with lamivudine alone after 24 weeks. Sixteen patients in the peg-interferon groups had HBSAg seroconversion compared to zero in the lamivudine only group.[62] A study in HBeAg-negative patients treated for 48 weeks found HBV DNA suppression was achieved in a higher proportion of patients on pegylated interferon monotherapy (19%) or combination lamivudine therapy (20%) as compared to lamivudine alone (7%) at 24 weeks post treatment.[28] Normalization of ALT was also higher in the peg-interferon groups (59% and 60%) versus lamivudine alone (44%).

Selection of therapy
Selection of therapy should be based on a variety of factors including efficacy, toxicity, availability, duration, route of administration, patient preference, provider preference, co-presence of HIV infection, and potential for resistance. For HBeAg(-) patients that require more than one year of therapy, lamivudine and telbivudine may be less optimal choices due to the potential for resistance after long treatment. For patients who are unable to be monitored closely, interferon therapy may not be optimal due to the many side effects and numerous laboratory studies required. For HIV positive patients, antiretroviral therapies may already provide suppression of HBV and additional therapy may not be required.

Treatment of HBV/HIV co-infection
Special considerations should be made to optimize therapy for patients who are co-infected with HIV and HBV. For co-infected patients who meet clinical indications for treatment of both HIV and HBV, the antiretroviral regimen should include agents that are active against both viruses. Tenofovir and either lamivudine or emtricitabine in combination with a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor is a good initial choice. For co-infected patients who do not meet clinical indications for treatment of HIV but require therapy for hepatitis B, interferon or adefovir can be utilized. Less is known about telbivudine, but it is thought to have no anti-HIV activity and could potentially be used. Lamivudine, emtricitabine, tenofovir and entecavir should not be given as monotherapy to an HIV/HBVinfected patient because HIV resistance mutations may develop. Acute hepatitis flare-ups can occur when HBV replication increases, such as when the antiretroviral regimen is changed and drugs active against HBV are discontinued. Therefore, the selection of HIV salvage regimens must take into account the HBV status of the patient. Flares can also occur when HBV develops resistance, or when antiretroviral therapy leads to an immune reconstitution inflammatory response (IRIS).

Monitoring and follow-up

Treatment success can be determined by monitoring for seroconversion of HBeAg in HBeAg(+) patients, appearance of anti-HBeAg, normalization of aminotransferases, viral suppression of HBV DNA, and histologic improvement. For patients treated with interferon, 16-24 weeks is ideal for HBeAg(+) patients while 12 months of therapy might be required for HBeAg(-) patients. Liver function tests can be monitored every 3 months during treatment and HBV DNA should be monitored every 3-6 months. One year after treatment, and every 3-6 months thereafter, patients should be tested for the eAg and anti-HBe. If seroconversion occurs, treatment should continue for at least 6 months after appearance of anti-HBeAg, then stopped. Sustained virologic suppression can be achieved in a significant number of HBeAg(+) patients who seroconvert. If seroconversion does not occur, treatment may be continued. If virologic breakthrough is present, the treating clinician may consider switching to another active agent. For HBeAg(-) patients optimal treatment duration is less clear but is usually one year or longer. Doses and common adverse effects for all anti-hepatitis B agents are presented in HBV 101.

Conclusions

Jails and prisons provide unique opportunities and challenges for the prevention, diagnosis, and treatment of chronic viral hepatitis. Improving hepatitis B management programs within correctional institutions has the potential to benefit the individual, the correctional population, and the larger public health. The optimal treatment of chronic HBV continues to evolve, especially in the HIV co-infected person.

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(continued from page 4)

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Resources

A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of Adults
http://www.cdc.gov/MMWR/preview/mmwrhtml/rr5516a1.htm

CDC's Viral Hepatitis B Website
http://www.cdc.gov/ncidod/diseases/Hepatitis/b/recs.htm

Hepatitis A, B, and C, Prevention Programs for Adult Correctional Facilities
http://www.hepprograms.org/adult/

Department of Health and Human Services 2007 Adult and Adolescent Antiretroviral Treatment Guidelines
http://aidsinfo.nih.gov/Guidelines/Default.aspx?MenuItem=Guidelines

National HIV/AIDS Clinician's Consultation Center
Warmline: National HIV Telephone Consultation Services
1-800-933-3413
PEPline: National Clincian's Post-Exposure Prophylaxis Hotline
1-888-448-4911
Perinatal Hotline: National Perinatal HIV Consultation and Referral Services
1-888-448-8765

CDC's Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

CDC's National HIV Testing Resource Website
http://www.hivtest.org/

CDC's Correctional Health Website
http://www.cdc.gov/correctionalhealth/

International AIDS Society-USA Panel
2006 Recommendations of the Treatment for Adult HIV Infection
http://jama.ama-assn.org/cgi/content/full/296/7/827

Center for Health Justice
http://healthjustice.net/

Community HIV/AIDS Mobilization Project
http://www.champnetwork.org/

American Correctional Health Services Organization
http://www.achsa.org/index.cfm

American Academy of HIV Medicine
http://www.aahivm.org/

SPOTLIGHT: THE 2008 CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS (CROI): A COMMUNITY PERSPECTIVE

IDCR invited Morris Jackson to report back from CROI on the issues that he found to be most significant for our readership. Mr. Jackson is the Treatment Education Coordinator with the Los Angeles based Center for Health Justice. He also serves as a community member on the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, and is a member of the AIDS Treatment Activist Coalition's (ATAC) Board of Directors and ATAC's Drug Development Committee.

I was again fortunate this year to be a CROI Community Educator Program Awardee recipient. As a PLWA/HIV and an advocate for the health care needs of the incarcerated, I had dual filters through which to interpret the data/findings presented and left with renewed vigor to make the information gleaned relevant and empowering to those who may not have been able to attend this meeting.

CROI is enormous in scope and it is impossible for one person to attend every session. The following is a brief synopsis of what I thought was some of the most interesting and 'correctionally' relevant data presented.

■ **Raltegravir (Isentress, MK-0528):** This agent is the first integrase inhibitor to receive FDA approval. Integrase inhibitors are a novel class of antiretrovirals. After the reverse transcription of HIV viral RNA into DNA is complete, integration of the HIV DNA into the host cell's DNA occurs. Integrase inhibitors work by blocking this process. Raltegravir, combined with optimized background therapy (OBT), was shown to offer durable efficacy and safety in patients with multiple-drug-resistant HIV and a history of treatment failure.[1,2] Many incarcerated HIV patients have exhausted treatment options, and raltegravir offers an additional tool for creation of salvage therapy for patients who have developed extensive resistance.

■ **Etravirine (Intelence, TMC 125):** Etravirine is the first non-nucleoside reverse transcriptase inhibitor (NNRTI) to receive FDA approval in the last 10 years. In treatment-experienced patients with multi-drug resistance, a regimen of etravirine plus OBT demonstrated greater viral load (VL) reduction and increase in CD4 counts compared to placebo plus OBT.[3,4] Etravirine is approved for treatment-experienced patients who have HIV that is resistant to multiple antiretroviral drugs. The FDA has not approved etravirine for use in treatment naive patients.

■ **Nevirapine:** Once-daily dosing of 400mg of the NNRTI nevirapine (Viramune, NVP) was shown to be as effective as 200mg twice-daily. Further, investigators concluded that "[f]or patients with detectable HIV RNA who have been exposed to other antiretroviral drugs, and commence a regimen including NVP, NVP once-daily, is associated with better and, a faster, virological suppression, as well as a stronger immune restoration (as compared to twice daily)." [5] Once-daily NVP may help decrease costs associated with medication administration in the correctional setting.

■ **Lopinavir/ritonavir (Kaletra):** Data was presented that demonstrated comparable tolerability and efficacy between 4 tablets once-daily and two tablets twice-daily of Kaletra (lopinavir /ritonavir).[6] The January 29, 2008, update of DHHS's federal treatment guidelines suggests that twice-daily Kaletra may be more suitable for those patients with high (> 100,000 copies/mL) pre-treatment viral loads.[7]

■ **HIV diagnosis and perceived transmission risk factors:** During the symposium "Curbing the US Epidemic," incarceration was cited as an important HIV transmission risk factor no less than six times, specifically in relation to the sexual network patterns and societal disparities of African-American women.[8] By extrapolation, this seemingly speaks to the need for improved prison/jail prevention efforts. Perhaps eradicating behavioral risk group (BRG) labeling in HIV testing is a beginning toward that end. For example, many male inmates do not identify themselves as MSM, and therefore do not perceive themselves at risk for contracting HIV and then transmitting it to their post-release female sexual partners. In a blinded serostudy of New York City jail entrants, most HIV infected inmates did not report recognized HIV risk factors.[9]

In a study of 21,419 adult prisoners entering the North Carolina Department of Corrections from January 2004 to May 2006, "associations between HIV serostatus and conventional HIV risk behaviors, mental health, co-infection status, and sociodemographic characteristics were estimated using logistic regression."[10] In this study, "approximately 40% of prisoners were voluntarily tested for HIV, and nearly 3.4% ... were HIV+." "Among men, HIV infection was most strongly associated with men who have sex with men (MSM) (OR 8.0), black race (OR 6.2), other non-white race (OR 7.4), and age 35 to 44 years (OR 4.1). The strongest risk factor among women was black race (OR 3.8)." The authors estimated that between 23% and 67% of HIV cases remained undetected. This study provided additional evidence that risk factor-based HIV testing in prison fails to diagnosis a significant number of those who are HIV-infected.

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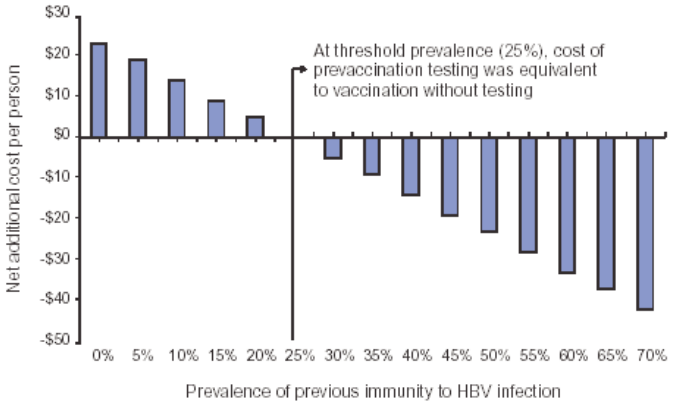
2. *Steigbigel R. Kumar P. Eron J. et al. 48-Week Results from BENCHMARK-2, a Phase III Study of Raltegravir in Patients Failing ART with Triple-class Resistant HIV. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 789.*
3. *Haubrich R. Cahn P. Grinsztein B. et al. DUET-1: Week-48 Results of a Phase III Randomized Double-blind Trial to Evaluate the Efficacy and Safety of TMC 125 vs Placebo in 612 Treatment-experienced HIV-1-infected Patients. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 790.*
4. *Johnson M. Campbell T. Clotet B. et al. DUET-2: Week-48 Results of a Phase III Randomized Double-blind Trial to Evaluate the Efficacy and Safety of TMC 125 vs Placebo in 591 Treatment-experienced HIV-1-infected Patients. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 791.*
5. *Calmy A. Nguygen A. Lang J. et al. Nevirapine Administered Once Daily Is as Efficient as Twice-daily Dosing. A Collaborative Cohort Study. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 786.*
6. *Gathe L. da Siva B. Loutfy M. et al. Study M05-730 Primary Efficacy Results at Week 48: Phase 3, Randomized, Open-label Study of Lopinavir/ritonavir Tablets Once Daily vs Twice Daily, Co-administered with Tenofovir DF + Emtricitabine in ARV-na_ve HIV-1-infected Subjects. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 775.*
7. *Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 29, 2008; 1-128. Available at http.www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed February 12, 2008. Page 22, Table 12.*
8. *Adimora A. What's Driving the US Epidemic among Women. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6, 2008; Boston, Massachusetts. Abstract 54.*
9. *Bennani Y. Parvez F. Forgione L. et al. Underdiagnosed HIV Infection among New York City Jail Entrants, 2006.. Results of a Blinded Serosurvey. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6 2008; Boston, Massachusetts. Abstract 539.*
10. *Rosen D. Wohl D. White B. et al. Characteristics and Behaviors Associated with HIV Infection in a Large Southern Prison System. Program and Abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6, 2008; Boston, Massachusetts. Abstract 550.*

IDCR-O-GRAM:

FIGURE. Cost effectiveness of prevaccination testing for immunity to hepatitis B virus (HBV) infection among jail and prison inmates — Texas, 2000–2002



Source: Texas Department of Criminal Justice.

Table 1: Recommended Doses of Currently Licensed Formulations of Adult Hepatitis B Vaccine, by Group and Vaccine Type

Single-antigen vaccine			Combination Vaccine			
	Recombivax HB®*		Engerix-B®†		Twinrix®†§	
Group	Dose (µg¶)	Vol. (mL)	Dose (µg¶)	Vol. (mL)	Dose (µg¶)	Vol. (mL)
Adults (aged ≥ 20 years)	10	1.0	20	1.0	20	1.0
Hemodialysis patients and other immunocompromised person ≥ 20 years	40**	1.0	40††	2.0	NA§§	NA

Source: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of Adults MMWR December 8, 2006 / 55(RR16); 1-25.

* Merck & Co., Inc., Whitehouse Station, New Jersey

† GlaxoSmithKline Biologicals, Rixensart, Belgium

§ Combined hepatitis A and hepatitis B vaccine, recommended for persons aged ≥ 18 years who are at increased risk for both hepatitis B and A virus infections

¶ Recombinant hepatitis B surface antigen protein dose

** Dialysis formulation administered on a 3 dose schedule at 0, 1, 2, and 6 months

†† Two 1.0-mL doses administered in 1 or 2 injections on a 4-dose schedule at 0, 1, 2, and 6 months

§§ Not applicable

Table 2: Guidelines for Postexposure Prophylaxis* of Persons with Nonoccupational Exposures‡ to Blood or Body Fluids that Contain Blood, by Exposure Type and Vaccination Status

Exposure	Unvaccinated§	Previously Vaccinated Person¶
HBsAg-positive source**		
Percutaneous (e.g. bite or needlestick) or mucosal exposure to HbsAg-positive blood or body fluid	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG)	Administer hepatitis B vaccine booster dose
Sex or needle-sharing contact of an HbsAg-positive person	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG)	Administer hepatitis B vaccine booster dose
Victim of sexual assault/abuse by a perpetrator who is HbsAg-positive	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG)	Administer hepatitis B vaccine booster dose
Source with unknown HbsAg status		
Victim of sexual assault/abuse by a perpetrator with unknown HbsAg status	Administer hepatitis B vaccine series	No treatment
Percutaneous (e.g. bite or needlestick) Or mucosal exposure to potentially Infectious blood or bodily fluids from a source With unknown HbsAg status	Administer hepatitis B vaccine series	No treatment
Sex or needle-sharing contact of an HbsAg-positive person	Administer hepatitis B vaccine series	No treatment

Source: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of Adults MMWR December 8, 2006 / 55(RR16); 1-25.

* When indicated, immunoprophylaxis should be initiated as soon as possible, preferably within 24 hours. Studies are limited on the maximum interval after exposure during which postexposure prophylaxis is effective, but the interval is unlikely to exceed 7 days for percutaneous exposures and 14 days for sexual exposures. The hepatitis B vaccine series should be completed.

‡ These guidelines apply to nonoccupational exposures. Guidelines for the management of occupational exposures have been published separately, and can also be used for the management of nonoccupational exposures if feasible.

§ A person who is in the process of being vaccinated but has not completed the vaccine series should complete the vaccine series and receive treatment as indicated.

¶ A person who has written documentation of a complete hepatitis B vaccine series and who did not receive post vaccination testing.

** Hepatitis B surface antigen.

Table 3: Typical Interpretation of Serologic Test Results for Hepatitis B Virus Infection

Serologic Marker				
HbsAg*	Total anti-HBc†	IgM§ anti-HBc	Anti-HBs¶	Interpretation
-**	-	-	-	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 ≥ 10 MIU/ML,*** passive transfer after hepatitis B immune globulin administration

Source: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of Adults MMWR December 8, 2006 / 55(RR16); 1-25.

* Hepatitis B surface antigen

† Antibody to hepatitis B core antigen

§ Immunoglobulin M.

¶ Antibody to HbsAg

** Negative test result

†† Positive test result

§§ To ensure that and HBsAg-positive test result is not a false positive, samples with repetedly reactive HBsAg results should be tested with a licensed (and, if appropriate, neutralizing confirmatory) test.

¶¶ Persons positive for only anti-HBc are unlikely to be infectious except under circumstances in which they are the source for direct percutaneous exposureof susceptible recipients to large quantities of virus (e.g., blood transfusions, organ transplant).

*** Milli-International Uni

HBV 101:

FDA Approved Medications for Prevention and Treatment of Hepatitis B Virus

Laboratory Assesment	Dose	Common adverse effects	Laboratory Assesment
interferon alfa-2b *Intron A* 3, 5, 10, 18, 25, 50 million IU Or peginterferon alfa-2a *Pegasys* 180 mcg/mL	HBeAg-positive patients: 5-6 million units SQ once-daily OR 9-10 million units SQ three times weekly x 4-6months HBeAg-negative patients: 5-6 million units SQ three times weekly x 12 months Peginterferon: 180 mcg SQ once weekly x 48 weeks	Anemia, granulocytopenia, thrombocytopenia, psychiatric disturbances (depression, suicide, psychosis), CNS effects such as seizures, ataxia, confusion, cardiac arrythmias, cardiomyopathy, myocardial infarction, hypotension, thyroid disturbances, renal failure, dermatologic disturbances, injection site reactions	Should not be used in patients with severe depression or unstable psychiatric disorders, uncontrolled thyroid disease or diabetes, in patients with ANC < 1.5 or platelets < 75 or in pregnant patients Monitor CBC, platelets, liver function tests, TSH, blood glucose, renal function every 4 weeks
lamivudine *Epivir-HBV* 100mg tablets	HBV monoinfected: 100mg orally once-daily HBV/HIV co-infected: 300mg orally once-daily, in combination with other agents to make a HAART regimen	Headache, fatigue, nausea, myopathy/myalgia, lactic acidosis, HBV flare upon abrupt discontinuation	Dose adjust in renal insufficiency
adefovir *Hepsera* 10mg tablets	10mg orally once-daily	Weakness, headache, nausea, abdominal pain, hematuria, renal dysfunction, HBV flare upon abrupt discontinuation.	Dose adjust in renal insufficiency
entecavir *Baraclude* 0.5 and 1mg tablets	Treatment naive: 0.5mg orally once-daily Lamivudine experienced: 1mg orally once-daily	Headache, fatigue, hyperglycemia, elevated lipase and amylase, hematuria, lactic acidosis, HBV flare upon abrupt discontinuation.	Dose adjust in renal insufficiency
telbivudine *Tyzeka* 600mg tablets	600mg orally once-daily	Fatigue, malaise, headache, abdominal pain, increased CPK, dizziness, lactic acidosis, myopathy, HBV flare upon abrupt discontinuation.	Dose adjust in renal impairment. Consider baseline and follow up CPK.

News and Literature Reviews

Additional News from the 2008 Conference on Retroviruses and Opportunistic Infections (CROI)

Resuming Therapy Doesn't Reverse Progression Risk of Off-and-On Therapy

Wafaa El-Sadr of the Harlem Hospital Center, New York presented additional data regarding the decision to halt the Strategies for Management of Anti-Retroviral Therapy (SMART) study. SMART, which ended two years ago, examined the impact of suspending antiretroviral therapy (ART) during periods of high CD4 counts. SMART consisted of two arms: one group continued ART throughout the study, while the other group discontinued ART when CD4 counts rose above 350/mm^3 and resumed ART when the CD4 count fell below 250/mm^3. The study was ended when it was determined that people in the interrupted ART group were at 1.8 times higher risk of death from any cause, as well as a 1.7 times higher risk of major cardiovascular, renal, or hepatic disease.

The interrupted group continued to experience worse health outcomes even after the study's termination in January 2006, at which time the investigators had counseled patients to resume uninterrupted treatment. Participants who had been assigned to the interrupted treatment group had a 24% higher risk of heart, kidney, or liver disease, a 37% higher risk of opportunistic disease or death, and a 41% higher risk of death than those in the control group of uninterrupted treatment. Members of the interrupted treatment group spent an average of 71% of the time on therapy, substantially less than the 91% of time spent on treatment in the control group. When researchers compared only people who had spent more than 85% of their time on ART, the risk of opportunistic infection or death appeared equivalent between the two groups.

Three factors were postulated to explain the disparity in health outcomes between the study's two arms. Some members of the interrupted treatment group did not resume ART therapy after the study's completion, thus limiting the effectiveness of treatment. Secondly, CD4 counts stayed lower in members of the interrupted treatment group, even if they did restart therapy. Finally, opportunistic diseases diagnosed before the study's completion may have had a long-term impact on the health of individuals. This study suggests that the impact of CD4-guided drug breaks may be long-lasting.

Mascolini, Mark. Resuming Therapy Can't Reverse Progression Risk With Off-and-On Therapy. 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008. Boston.

48-Week Results from BENCHMRK-2, a Phase III Study of Raltegravir (RAL) in Patients Failing Antiretroviral Therapy (ART) with Triple-Class Resistant HIV-1

Results from an ongoing double-blind Phase III study have demonstrated raltegravir's effectiveness in suppressing HIV viral loads. The study found that patients who took 400 milligrams of raltegravir twice daily in combination with optimized background therapy (OBT) had lower viral loads than patients whose treatment regimens included OBT and a placebo. The results were gathered after 48 weeks of treatment amongst patients living with HIV-1 in North and South America.

The success of this study offers hope to treatment-experienced individuals living with antiretroviral-resistant HIV, as well as the treatment-naive. Raltegravir, which acts as an HIV-1 integrase strand-transfer inhibitor, can be taken in combination with NRTIs, NNRTIs, PIs, and efuvirtide in order to combat multi-drug resistant strands of HIV. In addition, strains of HIV that become resistant to raltegravir may still remain sensitive to other types of antiretrovirals.

Levin, Jules. 48-Week Results from BENCHMRK-2, a Phase III Study of Raltegravir (RAL) in Patients Failing Antiretroviral Therapy (ART) with Triple-Class Resistant HIV-1. 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008. Boston.

Immediate Antiretrovirals During Acute OI Lower Death Risk: ACTG A5164

A Stanford University research team headed by Andrew Zolopa presented data from a randomized trial of 282 patients that evaluated whether or not to complete treatment of AIDS-related opportunistic infections (OI) before beginning ART in HIV-infected patients.

The study included individuals with acute OI including Pneumocystis pneumonia, bacterial pneumonia, cryptococcosis, Mycobacterium avium complex, or central nervous system toxoplasmosis. Participation was limited to patients who had never experienced antiretroviral failure and had not taken ART in the past 8 weeks or for more than 31 days in the past 6 months. The participants were evenly split into two treatment arms. While both groups received immediate treatment of their OI, one group also received immediate treatment with ART. The other group deferred ART until at least 28 days after enrollment in the study.

24.1% of those in the deferred group had a new AIDS diagnosis or had died, compared to 14.2% in the immediate treatment group. As such, participants who deferred antiretroviral treatment had twice the chance of progression as participants who began treatment immediately. Participants who received immediate treatment experienced a faster increase in CD4 count, thus limiting their period of vulnerability to new OIs or death. Differences in progression rates and death between the two groups were mainly limited to the first 6 months of the study, as there was little difference in the viral loads of the two groups by week 48. These findings emphasize the importance of immediate ART for patients suffering from acute AIDS-related OIs.

Mascolini, Mark. Immediate Antiretrovirals During Acute OI Lower Death Risk: ACTG A5164. 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008. Boston.

Sustained Virological Response to Interferon plus Ribavirin Reduces Liver-related Complications and Mortality in HIV/HCV Co-infected Patients

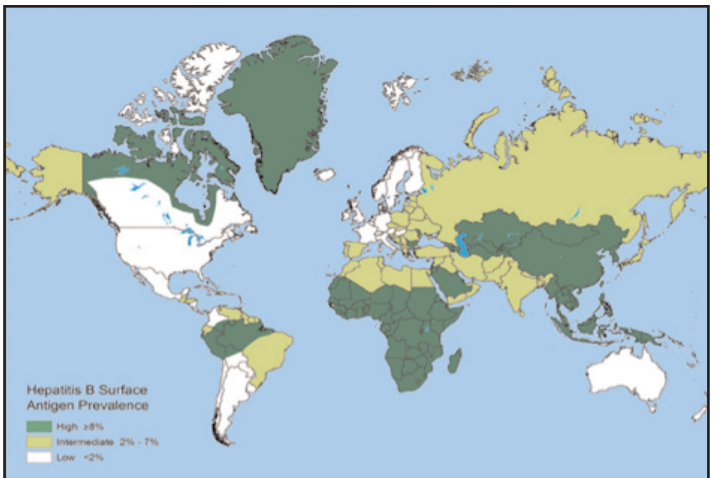
A recent analysis of the GESIDA 3603 Study Cohort provided new information on the impact of sustained virological response (SVR) on HIV/HCV coinfected patients. The study consisted of 711 patients who began interferon-ribavirin treatment between January 2000, and December 2005. Patients were seen every 6 months for 18 to 22 months, and clinical outcomes such as mortality, liver-related complications, and HIV progression were assessed. An estimated 31% of the study population achieved SVR during the course of this study. The health outcomes of this group were then compared to the remainder of the participants who did not achieve SVR.

Among the 218 people who achieved a SVR, the death rate was only .9%. This compared to a death rate of 6.9% among the 493 patients who did not achieve SVR. Liver related complications affected 3.7% of the non-SVR group and .5% of the SVR group. 2.2% of the non-SVR group had liver transplants, compared to 0% of the SVR-achieving group. In total, members of the non-SVR group had a 9 times greater risk of death, 20 times greater risk of liver decomposition, and 4 times greater risk of new AIDS conditions.

Levin, Jules. Sustained Virological Response to Interferon plus Ribavirin Reduces Liver-related Complications and Mortality in HIV/HCV-co-infected Patients. 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008. Boston.

Compiled by Christine Devore, Duke University

HBV World MAP



Prevalence of chronic infection with Hepatitis B virus, by country, 2006

Self-Assessment Test for Continuing Medical Education Credit - MEC #7256

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Medical Education Collaborative, Inc. (MEC) and *IDCR*. MEC is accredited by the ACCME to provide continuing medical education for physicians.

Medical Education Collaborative designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit™. The target audience for this educational program is physcians. Physicians should only claim credit commensurate with the extent of their participation in the activity. Statements of credit will be mailed within 6 to 8 weeks following the program.

Objectives:

- The leaner will be able to describe the recommended treatment, dosing, and monitoring options for the treatment and management of the hepatitis B virus.
- The learner will be able to explain the prevention, screening, and diagnosis measures for the hepatitis B virus.
- The learner will be able to discuss the most significant studies presented at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI).

1. Which of the following is NOT a recommended schedule for hepatitis B vaccination?

A. 0,1, and 6 months
B. 0, 1, and 4 months
C. 0, 1, and 5 months
D. 0, 1, 2, and 12 months
E. None of the above

2. The CDC recommends that an unvaccinated victim of sexual assault/abuse by a perpetrator with unknown HbsAg status does NOT need to be treated with hepatitis B postexposure prophylaxis.

TRUE or FALSE

3. Which of the following is a factor which selection of therapy for a hepatitis B positive patient should be based upon?

A. Efficacy
B. Potential of resistance
C. Toxicity
D. Patient and provider preference
E. All of the Above

4. In a study by Rosen et al. of adult prisoners entering the North Carolina Department of Corrections, the authors estimate that between 23% and 67% of HIV cases remained undetected.

TRUE or FALSE

5. Which of the following medications approved for the treatment of hepatitis B virus should NOT be taken by patients with severe depression or unstable psychiatric disorders?

A. Lamivudine
B. Entecavir
C. Interferon
D. Both A and C

In order to receive credit, participants must score at least a 75% on the post test and submit it along with the credit application and evaluation form to the address/fax number indicated. Statements of credit will be mailed within 6-8 weeks following the program.

Instructions:

- Applications for credit will be accepted until March 26, 2009.
- Late applications will not be accepted.
- Please anticipate 6-8 weeks to recieve your certificate.

MEDICAL EDUCATION COLLABORATIVE®
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Please print clearly as illegible applications will result in a delay.

Name: _____ Profession: _____

License #: _____ State of License: _____

Address: _____

City: _____ State: _____ Zip: _____ Telephone: _____

Please check which credit you are requesting ___ ACCME or ___ Non Physicians

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I certify that I participated in IDCR monograph February/March 2008 Issue

Please fill in the number of actual hours that you attended this activity.

Date of participation: _____

Number of Hours (max. 1): _____

Signature: _____

Please Submit Completed Application to:

Medical Education Collaborative
651 Corporate Circle, Suite 104, Golden CO 80401
Phone: 303-420-3252 FAX: 303-420-3259
For questions regarding the accreditation of this activity, please call 303-420-3252

COURSE EVALUATION - MEC #7256

I. Please evaluate this educational activity by checking the appropriate box:

Activity Evaluation					
	Excellent	***Very Good***	***Good***	***Fair***	***Poor***
Faculty					
Content					
How well did this activity avoid commercial bias and present content that was fair and balanced?					
What is the likelihood you will change the way you practice based on what you learned in this activity?					
Overall, how would you rate this activity?					

II. Course Objectives

Were the following overall course objectives met? At the conclusion of this presentation, are you able to:

- The learner will be able to describe the recommended treatment, dosing, and monitoring options for the treatment and management of the hepatitis B virus. **YES NO SOMEWHAT**
- The learner will be able to explain the prevention, screening, and diagnosis measures for the hepatitis B virus. **YES NO SOMEWHAT**
- The learner will be able to discuss the most significant studies presented at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI). **YES NO SOMEWHAT**

III. Additional Questions

a. Suggested topics and/or speakers you would like for future activities.

_____

b. Additional Comments

_____

SAVE THE DATES

2008 National STD Prevention Conference
Chicago, IL
March 10-13, 2008
Visit: http://www.cdc.gov/stdconference/default.htm

Infectious Diseases: Adult Issues in the Outpatient and Inpatient Settings
Sarasota, FL
March 10-14, 2008
Visit: http://www.ams4cme.com

Strengthening Connections between Parents and Children Affected by Substance Abuse, HIV and Incarceration
San Francisco, CA
March 12-14, 2008
Visit: http://aia.berkeley.edu/strengthening_connections/index.html

HIV Testing of Defendants of Felony Sexual Assault
March 13, 2008
Satellite Conference, NY State
Visit: http://www.nyhealth.gov/diseases/aids/training/broadcast/index.htm

International Conference on Emerging Infectious Diseases
Atlanta, GA
March 16-19, 2008
Visit: http://www.iceid.org/

2nd Annual Academic and Health Policy Conference on Correctional Health
Boston Marriott, Quincy, MA
March 27-28, 2008
Visit: http://www.umassmed.edu/Correctional_Health_Conf/index.aspx

Rapid HIV Testing & Diagnosing Acute HIV Infection Satellite Videoconference & Webcast
April 18, 2008
12:30-2:30 p.m. (ET)
CME's & Nursing credits, No Fees
Visit: www.amc.edu/hivconference
(518) 262-4674
ybarraj@mail.amc.edu

16th Texas HIV/STD Conference
May 15-22, 2008
Austin, TX
Visit: http://www.dshs.state.tx.us/hivstd/conference/2008/default.shtm

Updates in Correctional Health Care
San Antonio, TX
May 17-20, 2008
Viist: http://www.ncchc.org/education/index.html

HIV/AIDS 2008:
The 20th Annual National Conference on Social Work and HIV/AIDS
Washington D.C.
March 22-25, 2008
Visit: http://socialwork.bc.edu/outreach/hiv-aids

2008 HIV Prevention Leadership Summit
Detroit, MI
June 11-14, 2007
Visit: http://nmac.org/conferences___trainings/HPLS/