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Hepatitis B Virus Infection in US Correctional Facilities: A Review of Diagnosis, Management, and Public Health Implications

Shaili Gupta and Frederick L. Altice

ABSTRACT *Among the blood-borne chronic viral infections, hepatitis B virus (HBV) infection is one that is not only treatable but also preventable by provision of vaccination. Despite the availability of HBV vaccine for the last 15 years, more than 1.25 million individuals in the USA have chronic HBV infection, and about 5,000 die each year from HBV-related complications. From a societal perspective, access to treatment of chronic viral infections, like HIV and viral hepatitis, is highly cost-effective and has lasting benefits by reducing risk behaviors, morbidity, mortality, as well as disease transmission in the community. Individuals in correctional facilities are specially predisposed to such chronic viral infections because of their high-risk behaviors. The explosion of incarceration in the USA over the last few decades and the disproportionate burden of morbidity and mortality from chronic infections among the incarcerated have put incredible strains on an overcrowded system that was not originally designed to provide comprehensive medical care for chronic illnesses. Recently, there has been a call to address medical care for individuals with chronic medical conditions in correctional settings, including those with infectious diseases. The economic and public health burden of chronic hepatitis B and its sequelae, including cirrhosis and hepatocellular carcinoma, is felt most prominently in managed care settings with limited budgets, like correctional facilities. Prevalence of HBV infection among the incarcerated in the USA is fivefold that of the general population. We present a review of diagnosis, prevention, and the recently streamlined treatment guidelines for management of HBV infection in correctional settings, and discuss the implications and public health impact of these measures.*

KEYWORDS *Prisons, Hepatitis B virus, Chronic hepatitis B, Treatment of HBV, HIV, Injection drug users, Correctional institutions, Lamivudine, Entecavir, Treatment guidelines, Cost–benefit*

THE EPIDEMIC OF INCARCERATION

In the USA, at year end 2006, over 7.2 million people were under correctional supervision and over 2 million were housed within correctional institutions, resulting in 3.4% of all US adult residents (one in every 31 adults) being under correctional supervision.[1] The USA imprisons its population at the highest known rate in the world, at 751 per 100,000 in 2006, indicating the country's formidable

Gupta and Altice are with the Section of Infectious Diseases, AIDS Program, Yale University School of Medicine, New Haven, CT, USA.

Correspondence: Shaili Gupta, Section of Infectious Diseases, AIDS Program, Yale University School of Medicine, 135 College Street, Suite 323, New Haven, CT 06510-2283, USA. (E-mail: shailigupta@gmail.com)

social policy of imprisonment and the huge public health impact of prisoners' health on communities at large.[2]

Inmates in correctional facilities bear a greater burden of chronic viral infections, substance use disorders, mental illness, and sexually transmitted diseases.[3] Women prisoners are at additional risk for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), as a consequence of being more likely to be drug users and engaging in commercial sex work.[4] The most recent report of the burden of infectious diseases among prisoners and recently released individuals in the USA was presented to the Congress with data accurate to 1996, indicating disproportionately higher prevalence of chronic infections among these individuals than the general US population: HIV (ninefold higher), AIDS (sixfold), HCV (tenfold), HBV (fivefold), and tuberculosis (fourfold).[5] Access to prevention and medical treatment during incarceration and continuity after release can provide lasting benefits to communities by reducing disease transmission and by facilitating rehabilitation.[6,7]

EPIDEMIOLOGY OF CHRONIC HEPATITIS B INFECTION

More than 2 billion people worldwide have been infected with HBV, of whom 360 million are chronically infected and are at an increased risk of liver-related sequelae, including cirrhosis, fulminant hepatic failure, hepatocellular carcinoma (HCC), and a 15–25% higher risk of premature death.[8] In the USA, the prevalence of HBV infection (including persons with chronic infection and those with previous infection) was 4.9% in the third National Health and Nutrition Examination Survey (NHANES III, 1988–1994).[9] The incidence of acute HBV infection has declined in the USA over the last 15 years because of routine HBV vaccination of infants. Still, in 2006, an estimated 1.25 million individuals had chronic HBV infection, and 46,000 new cases of HBV infection were estimated to have occurred in that year alone —2.4 times as many as the newly diagnosed cases of hepatitis C.[10] It is estimated that up to 5,000 people die each year in the USA from HBV-related complications.

Up to 40% of all Americans with chronic viral hepatitis and approximately 30% of persons with acute HBV infection have been incarcerated.[11] Among patients with acute hepatitis B reported to the CDC, 5.6% have a history of incarceration during the disease incubation period.[12] HBV infection is known to be transmitted within correctional settings, and incidence rates have ranged from 0.82% to 3.8% per year.[13,16] Outbreaks of HBV in correctional facilities have been well-documented.[5,14–16] The source-patient as well as many of the infected inmates in these outbreaks were found to have subclinical infection, indicating the undetected burden of disease. Such subclinical transmission risk among the incarcerated population formed the basis of recommendation by CDC for HBV vaccination in correctional settings.

An accurate prevalence of HBV infection in US correctional facilities has not been ascertained for more than a decade.[5] At that time, in 1996, HBsAg seroprevalence was ~2% among this population, as compared to the national prevalence of 0.4% and had been estimated based on two state studies in California (1994) and New York (1987–1997).[17,18] The prevalence of serologic markers for current or past HBV infection among inmates ranges from 13% to 47%. Prevalence is higher among female prisoners (37–47%) than in men (13–32%).[17,19] Upon release, susceptible inmates are often at increased risk for infection because they

resume high-risk behaviors. A study of recidivist women reported an HBV seroconversion rate of 12.2/100 person-years between incarcerations, compared with estimated incidence of 0.03/100 person-years for the US population.[19,20] Prisons are, therefore, important sites for detection of and vaccination against hepatitis B, particularly in women to prevent perinatal transmission of HBV infection to newborns. A survey of US correctional institutions confirmed the lack of routine HBV screening despite the public health mandate to vaccinate high-risk individuals as well as to identify and treat individuals with active HBV infection.[21] Of the 35 states that responded to that survey, only two reported screening all their inmates routinely for hepatitis B immunity to determine requirement for vaccination. Two other states offered HBV vaccine to all inmates without routine screening.

NATURAL HISTORY OF HBV, CLINICAL SPECTRUM, AND LABORATORY VALUES

After an initial incubation period of 1 to 4 months, 30% to 80% exposed adults develop symptomatic acute hepatitis B with fatigue, nausea, and occasionally jaundice.[22] Laboratory testing reveals significant elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which normalize within 1 to 4 months in patients who recover. Serologic markers are diagnostic (Table 1).

Progression to chronic hepatitis is defined as persistence of elevated AST/ALT or HBsAg for more than 6 months and is seen in only 5% of immunocompetent adults infected with HBV.[22] Persistence of HBsAg marks transmission risk of infection, which is markedly increased with HBeAg positivity. During the initial immunotolerant phase, serological markers of viral replication including HBsAg, HBeAg, and HBV DNA are seen, while AST/ALT are normal to mildly elevated. Subsequently, there is a prolonged immune-clearance phase of chronic active hepatitis (CAH) with normal to moderate elevation of AST/ALT and gradual reduction in the HBV DNA level. Spontaneous HBeAg seroconversion occurs at a rate of 10% to 20% per year in healthy adults and is marked by elevation of AST/ALT, with clinical worsening. Persons who have been exposed to HBV just before incarceration, therefore, may not develop clinical symptoms until some time after incarceration. These symptoms of lethargy, nausea, abdominal pain, and occasionally mild fevers may be mistaken for those of withdrawal from illicit drugs. Liver function tests and serological evaluation can help discern substance withdrawal from HBV infection in these inmates for appropriate management.

Less than 1% adult patients clear the HBsAg per year (known as HBsAg-seroconversion). In most, it persists but with undetectable HBV DNA. Even in these "healthy carriers", there is underlying slow histopathological viral activity, with progressive fibrosis and increased risk for HCC.[23] Patients with negative HBeAg and undetectable HBV DNA should therefore have regular follow-up until HBsAg-seroconversion occurs.[45]

HEPATITIS B VIRUS GENOTYPES AND MUTANTS: IMPLICATIONS ON CLINICAL OUTCOME AND TREATMENT

Eight different genotypes of HBV (A–H) are known to date. In the USA, the commonest genotypes are A and C, followed by B and D.[24] HBV genotype correlates to clinical outcome. For instance, genotype C increases the risk for HCC.[25] Genotype B is associated with HBeAg seroconversion at a younger age,[26]

TABLE 1 Determination of HBV infection status by serological markers

Interpretation	Serological Markers							ALT
	HBsAg	Anti-HBs	IgM anti-HBc	Total anti-HBc	HBeAg	Anti-HBe	HBV DNA	
Susceptible	−	−	−	−	−	−	−	Normal
Early incubation period	+	−	−	−	−	−	+/−	Normal/Elevated
Acute hepatitis B	+	−	+	+	+	−	+	Elevated
Resolving acute hepatitis	−	−	+	+	+/−	+/−	+/−	Normal/Elevated
Immunity from vaccination	−	+	−	−	−	−	−	Normal
Immunity from infection	−	+	−	+	−	+/−	−	Normal
Chronic HBeAg+ hepatitis B	+	−	−	+	+	−	+	Elevated
Chronic HBeAg− hepatitis B	+	−	−	+	−	+	+	Elevated
Low-level chronic infection	−	−	−	+	−	+/−	+	Normal
Healthy carrier	+	−	−	+	−	+/−	−	Normal
False positive/past infection	−	−	−	+	−	−	−	Normal

while genotypes A and B are associated with improved response to interferon therapy.[27] To date, response to antiviral agents has not been correlated with HBV genotype.

HBV has the highest mutability among all DNA viruses. Certain mutations result in complete prevention or down-regulation of HBeAg production, thereby increasing the virulence. HBV strains with these mutations are known as Precore and Core Promoter mutants, respectively. Such mutants can result in failure of immunological attempts at HBeAg/Ab-seroconversion and cause relatively severe histopathological disease, albeit low HBV DNA levels. This plays a role in the determination of time for treatment initiation (Table 4). The risk of cirrhosis is higher in HBeAg-negative disease, with up to 29% cirrhotic at the time of initial presentation.[28] HBV also develops mutations under selective pressure from antivirals, as outlined later.

PROGNOSIS OF HBV INFECTION

The morbidity and mortality in chronic hepatitis B are directly related to the development of cirrhosis and HCC. Cirrhosis develops within 6 years in 30% of patients with moderate CAH and within 4 years in 50% of those with severe CAH.[29] In patients with HBV-related cirrhosis, the probability of decompensation is 20% to 28% and that of HCC is 6%, 5 years after diagnosis.[29] One large study found that the relative risk of HCC was 9.6 among patients with HBsAg alone and 60.2 among those with both HBsAg and HBeAg, as compared with those who were negative for both.[30] Elevated serum HBV DNA level ($\geq$10,000 copies/mL) is a strong risk predictor of adverse outcomes independent of HBeAg and serum ALT level, with a cumulative incidence rate of 14.9% for HCC and relative risk of 6.5 for cirrhosis at HBV DNA level of $\geq$1 million/mL.[31,32] Co-infections with HIV, HCV, both HIV and HCV, and with HDV have been shown to increase the rates of cirrhosis and HCC.[46] Host HLA type also predicts outcome of infection. HLA DR13 promotes a robust immune response with spontaneous clearance of HBV and HLA-DRB1*07 reduces the response to interferon therapy for HBV.[33,34]

PREVENTION OF HBV INFECTION IN CORRECTIONAL FACILITIES

Many adolescents and young adults are still not receiving vaccinations, despite recommendations for universal vaccination among persons aged $\leq$18 years[35] and will likely put themselves at risk for HBV infection through sexual and drug-use

TABLE 2 Postexposure prophylaxis for HBV after percutaneous/mucosal exposures

HBsAg seropositivity status of source individual	HBV vaccination status of exposed individual	Recommended prophylaxis
Seropositive	Unvaccinated	Vaccine series + 1 dose HBIG
Seropositive	Vaccinated	1 Booster dose vaccine
Unknown	Unvaccinated	Vaccine series
Unknown	Vaccinated	No treatment

HBV hepatitis B virus, *HBIG* hepatitis B immunoglobulin

behaviors.[36] Such high-risk behavior is especially common in the incarcerated population.[37] Transmission of blood-borne pathogens including HBV among inmates is known to occur during injection drug use, sharing tattoo paraphernalia and razor blades, fights, and consensual/nonconsensual sexual activity.[38] HBV is known to be secreted in saliva and to survive on environmental surfaces for at least a week, with potential transmission by sharing contaminated personal use items such as razors and toothbrushes—all of which are in limited supply within correctional settings.[39,40] Lack of easy access to condoms and needle-exchange programs enhances the risks involved in these settings.

Provision for both pre-exposure and post-exposure prophylaxis is required to maximize prevention of HBV transmission in correctional facilities. Recently updated recommendations of Advisory Committee on Immunization Practices (ACIP) include hepatitis B vaccination for all adults in high-risk individuals, including inmates of correctional facilities.[41] The recommended vaccination schedule consists of three intramuscular doses of hepatitis B vaccine given at 0, 1, and 6 months. Better response to the vaccine in HIV-positive inmates can be ensured by giving the vaccine when CD4 cell counts are >200/μL and by giving double-dose vaccines.[42,45] Post-exposure prophylaxis for non-occupational exposure (for inmates) depends on HBV vaccination/infection status of the exposed and source individuals (Table 2) and should be initiated as soon after exposure as possible to maximize the effectiveness.[41] Pregnancy is not a contraindication for the hepatitis B vaccine. Vaccination of women inmates of reproductive age is of special significance to prevent perinatal HBV transmission. If universal vaccination is not implemented, vaccination of high-risk inmates could still bring about reasonable changes in the burden of disease and morbidity. For instance, inmates infected with HIV and/or HCV should be screened for HBV infection and, if found to be seronegative, should be vaccinated to prevent the accelerated hepatic fibrosis caused by HBV co-infection in these individuals.

The challenges for HBV vaccination vary between prisons and jails. While it is both cost-effective and feasible to screen and vaccinate prisoners due the longer period of incarceration, jails pose more challenging constraints with the high number of entrants and the rapid turnover of the population. In such settings, it may be useful to implement an accelerated immunization schedule (HBV vaccine at 0, 7, and 21 days or at 0, 1, and 2 months).[43] Protective levels of antibody have been demonstrated after one (30–50%) or two (89%) doses of the vaccine.[44]

TREATMENT OPTIONS AND STATE OF THE ART MANAGEMENT

Treatment guidelines are continually evolving with expansion of knowledge about natural history and development of new therapies. Two sets of guidelines are commonly used, the AASLD practice guidelines[45] and a treatment algorithm developed by a group of expert hepatologists in the USA.[46]

Candidacy for treatment initiation and choice of medications are determined by clinical and biochemical/serological evaluation (Table 3). The two sets of guidelines differ in cutoff limits for HBV DNA and ALT levels in determining treatment eligibility (Table 4). Both sets of guidelines make special note of the corrected upper limits of ALT at 30 IU/L for men and 19 IU/L for women. With growing evidence that progressive liver fibrosis can occur even with normal ALT levels, more experts recommend not basing treatment on ALT levels alone.[31,32,46] Liver biopsy is most

useful in patients for whom treatment eligibility is unclear and for patients older than 35–40 years of age with normal ALT levels, a group that may be at higher risk for fibrosis. If liver histopathology shows significant fibrosis in these individuals, treatment may be indicated even if ALT levels are low or within normal limits.

Several new and effective treatments for HBV infection have resulted in the ability to improve HBV treatment outcomes and potentially result in reduced transmission of HBV.[47] Currently, seven therapeutic agents are approved for the treatment of adults with chronic hepatitis B in USA interferon alpha-2b, peginterferon alpha-2a, lamivudine, adefovir dipivoxil, entecavir, telbivudine, and tenofovir.[45] Tenofovir is the most recently added agent to this list, after it was approved for the treatment of chronic HBV infection by FDA in August, 2008. Clevudine and emtricitabine are fast gaining data to support approval as first line agents for treatment of HBV infection. Entecavir and tenofovir have superior efficacy and comparable safety to lamivudine and adefovir.[48,49] Tenofovir is safe and efficacious in HBV-infected cirrhotic patients, too.[50] In HBeAg-positive individuals, HBsAg loss occurs at rates of 3% and 5%, respectively, with tenofovir and entecavir.[51,52] Interferons result in excellent HBsAg seroconversion rate (29%), but the rate of sustained virological response is lower (26%) and incidence of adverse effects higher.[53]

TABLE 3 Suggested Evaluation of inmates with chronic hepatitis B

Initial evaluation	
Clinical	1. Medical/family history: Determine potential risk exposures 2. Physical examination: Look for signs of cirrhosis (ascites, edema, gynecomastia, palmar erythema, spider angiomas)
Biochemical	CBC[a], LFTs, Coagulation profile, Creatinine.
Serological	HBe antigen/antibody, HBV DNA, HBV-genotype[b]
Coinfection screening	Antibodies against HIV, HCV, HAV
Complication screening	AFP, liver ultrasound[b] (if AFP or clinical suspicion high)
Histopathological	Liver biopsy[b]
Follow-up evaluation for those on treatment	
Clinical (Q 3 months)	1. Physical examination: Look for signs of worsening liver disease/cirrhosis. 2. Counseling to avoid risk behavior, and encourage medication adherence.
Biochemical	CBC[a], LFTs every 3 months, Coagulation profile every 6 months
Serological (Q 3–6 months)	HBV DNA, HBe Antigen/Antibody if HBeAntigen positive hepatitis
Radiological	Liver ultrasound[b] (if sudden decompensation occurs)
Follow-up evaluation for those not on treatment (initially did not qualify for treatment)	
Clinical (Q 3 months)	1. Physical examination: Look for signs of worsening liver disease/cirrhosis 2. Counseling to avoid risk behavior
Biochemical	LFTs every 3–6 months, if were normal initially.
Serological	HBV DNA every 6 months, if was low initially.
Radiological	Liver ultrasound[b] (if Sudden decompensation occurs)

CBC complete blood count, *LFTs* liver function tests, *HBV DNA* hepatitis B virus deoxynucleic acid, *HIV* human immunodeficiency virus, *HCV* hepatitis C virus, *HAV* hepatitis A virus, *AFP* alpha fetoprotein, *Q* every

[a]Platelet count should especially be monitored in CBC profile

[b]Optional, depending on clinical judgment. Generally recommended by AASLD guidelines

TABLE 4 Treatment guidelines for chronic hepatitis B

HBe Ag	HBV DNA[a]	ALT[b]	AASLD treatment guidelines[d]	US hepatologists treatment algorithm[d]
+	<20,000	Normal	Observe. Monitor ALT/HBeAg q6-12 months[e]	Observe. Monitor ALT/HBeAg q6-12 months[e]
+	≥20,000	Normal[c]	Observe. Monitor ALT/HBeAg q6-12 months[e]	Consider biopsy, treatment if age>40 or ALT >ULN
+	≥20,000	1–2× ULN[c]	Consider biopsy, treatment if age>40 and ALT persistently high	Treat[f]
+	≥20,000	≥2× ULN	Treat[f]	Treat[f]
−	<2,000	Normal	Observe. Monitor ALT/HBVDNA q6–12 months[e]	Observe. Monitor ALT/HBVDNA q6–12 months[e]
−	2,000–20,000	Normal[c]	Observe. Monitor ALT/HBVDNA q6–12 months[e]	Consider biopsy; treat if disease present. Or monitor ALT for increase
−	2,000–20,000	1–2× ULN[c]	Monitor ALT/HBVDNA q3mon. Consider Biopsy	Treat[f]
−	≥20,000	≥2× ULN	Treat[f]	Treat[f]
+/−	<2,000	Cirrhosis compensated	Consider treatment especially if ALT elevated. ADV or ETV are preferred agents	
+/−	≥2,000	Cirrhosis compensated	Treat. Combination therapy preferred (LAM + ADV, or LAM + ETV, or ADV +ETV)	
+/−	Any	Cirrhosis decompensated	Refer for transplant and treat with ADV + LAM, or ADV + ETV (combination therapy)	

[a]Values shown in IU/mL (1 IU/mL is equivalent to approximately 5.6 copies/mL)

[b]The upper limit of normal (ULN) for serum ALT concentrations for men and women are 30 IU/L and 19 IU/L, respectively

[c]Differences in Recommendations from AASLD and US Hepatologists' Guidelines

[d]Liver biopsy is strongly recommended before initiating treatment

[e]On initial diagnosis, every 3 months for 1 year to ensure stability

[f]PegIFNα-2a, ETV, ADV are preferred over LAM because of high risk for resistance with lamivudine treatment. Choose antiviral if HBV DNA high or Genotype D. Choose PegIFNα-2a if Genotype A. Pretreatment genotype testing is not a standard recommendation at this time, but may be useful in patients with high-level viremia and significant liver disease, to help determine the most appropriate agent

ADV Adefovir, *ETV* Entecavir, *LAM* Lamivudine, *IFN* Interferon

The overall duration of treatment for many patients is still uncertain, as none of the currently available agents eradicate HBV DNA indefinitely. In HBeAg-positive hepatitis, treatment is continued until ≥3–6 months after HBeAg seroconversion. Virologic response is sustained in 70–90% patients after treatment discontinuation. For HBeAg-negative infection, the duration of treatment is prolonged and indefinite. Medications with a high genetic barrier to resistance, e.g., entecavir, are therefore preferred. Early virologic response is defined as a decrease in HBV DNA level by ≥1 log 10 IU/ml at 12 weeks of treatment. HBV DNA level at 24 weeks of treatment is the best predictor of efficacy. Experts recommend assessing on-treatment virologic response every 3 months until sustained aviremia, and adding a more potent agent if response is inadequate.[54] The risks and benefits of long-term treatment of chronic HBV infection are largely unknown at this time. Lamivudine and adefovir, the earliest antiviral agents used for HBV, have been shown to be safe and effective over prolonged periods of time but are riddled with development of breakthrough antiviral resistance.

Management of chronic HBV infection within correctional facilities needs to be supervised by physician experts, with careful and strategic patient selection and close monitoring. The evidence-based data that direct treatment guidelines are not derived from studies of inmate populations. Many of the critical studies involved East Asian populations, not largely represented in US jails and prisons. Expert evaluation is therefore required before making treatment decisions. Caution is required when planning premature discontinuation of treatment before adequate seroconversion has occurred. Severe acute exacerbation of hepatitis has been reported when patients discontinue anti-HBV agents. This is of special significance in inmates who are known to be poorly adherent to treatment. Medication reconciliation is important in this matter for inmates entering jails/prisons on treatment and those transferring between correctional facilities.

ANTIVIRAL RESISTANCE AND COMBINATION THERAPY

Monotherapy with lamivudine is associated with unacceptably high rates of resistance (14–32% per year and 70% after 4 years).[55] In patients coinfected with HIV, this rate is higher (≤90% after 4 years).[56] Lamivudine monotherapy is therefore not currently indicated for treatment of chronic hepatitis B, with the exception of pregnant patients. Lamivudine in combination with adefovir may be used in cirrhotic patients, who cannot tolerate pegylated interferon, entecavir, or tenofovir. Adefovir resistance develops in up to 3% of HBeAg-positive patients and 5.9% of HBeAg-negative patients.[57,58] Telbivudine monotherapy results in genotypic mutations with virologic rebound in 21.6% of HBeAg-positive and 8.6% of HBeAg-negative patients within 2 years.[59] Tenofovir and clevudine have lower incidence of resistance[60,61] and entecavir has the lowest resistance rate (<1%).[62] Tenofovir is effective in those who have developed resistance to lamivudine.[63] In those with adefovir resistance, combination therapy with tenofovir and emtricitabine is potently more effective than tenofovir monotherapy.[64,65] The role of combination therapy in treatment-naive individuals is being investigated. Adefovir in combination with lamivudine or emtricitabine has been shown to be more effective than monotherapy with lamivudine or adefovir.[66,67]

Pretreatment genotypic resistance testing in treatment-naïve persons is not routinely recommended at this time but may become important in the future to help determine appropriate treatment options.

HBV TREATMENT IN SPECIAL GROUPS

Pregnancy. Lamivudine, entecavir, and adefovir are category C drugs, but the larger experience with lamivudine has made it the agent of choice for HBV treatment in pregnancy and has been shown to decrease vertical transmission.[68] Adefovir is avoided because it is embryotoxic and teratogenic in mice, at doses that attain serum levels 38 times that in humans, although it is safe at lower doses.[69] If disease is mild, treatment may be delayed until after pregnancy. Regardless of treatment during pregnancy, perinatal immunoprophylaxis is crucial to minimize the risk of HBV-related disease in the neonate.

HIV/HBV coinfection. Prevalence of coinfection is predicted to be high in the incarcerated population. In the USA, about 10% of HIV-positive persons are coinfected with HBV, and liver-related mortality in these patients is 17 times that for HBV-monoinfected patients.[70] Coinfected persons have higher and prolonged HBV viremia and HBeAg seropositivity, with relatively lower ALT levels.[71] Tenofovir, with emtricitabine or lamivudine, is a frequent component of antiretroviral regimens when both infections need treatment. Current treatment guidelines for HIV recommend that all HIV-infected individuals who need treatment for HBV infection should be started on a fully suppressive regimen for both infections, regardless of their CD4 counts or HIV viral loads.[72] In case HIV treatment is not an option or is refused by the patient, HBV infection can be treated by using pegylated interferon-2α, which has no activity against HIV. Adefovir is another option for such individuals because of its lack of activity against HIV at a dose of 10 mg, which is used for treatment of HBV. Entecavir can induce M184V mutation in HIV when used as single antiviral in coinfected patients and is therefore avoided for HBV monotherapy in the coinfected.[73] Telbivudine has not been shown to target HIV but is not preferred for HBV treatment in coinfected patients.[45] Special caution is required in treatment of coinfected individuals with antivirals effective against both HIV and HBV. If changes in HIV genotypic resistance pattern warrant modification in the antiretroviral therapy, care should be taken not to discontinue drugs that are effective against HBV without substituting another agent with anti-HBV activity, unless the patient has achieved HBeAg seroconversion and adequate consolidation treatment. Sudden discontinuation of anti-HBV agent in patients who have not yet seroconverted can result in acute exacerbation of hepatitis.

HBV/HCV coinfection. HBV/HCV coinfection causes accelerated progression of hepatic fibrosis and higher incidence of HCC.[74] Most HBV/HCV coinfected patients have higher HCV RNA levels with predominance of that infection and lower HBV DNA levels with absence of HBeAg. Treatment should be initially directed at the virus that is more clinically and virologically dominant, with addition of therapy for the other virus if required. Peginterferon/ribavirin is the recommended regimen when both HCV and HBV are codominant.[46] Suboptimal HBV response or breakthrough HBV viremia warrants addition of entecavir or adefovir.[75]

Cirrhosis. These patients usually qualify for treatment regardless of the viral load and ALT levels. Combination therapy is preferred, with the agents of choice being adefovir or entecavir in combination with lamivudine. Those with decompensated cirrhosis should be referred for liver transplant as well. Current guidelines suggest that all individuals with HBsAg seropositivity and cirrhosis, regardless of their HBV viremia, should be screened for HCC by checking serum alpha fetoprotein (AFP)

and liver ultrasound examinations every 6–12 months.[76] Special groups of HBsAg-positive individuals recommended for HCC screening, even in the absence of cirrhosis, are Asians, HIV- or HCV-coinfected individuals, Africans over age 20, those with family history of HCC, and those with very high-level HBV viremia and ongoing hepatic inflammatory activity.[76]

CONTINUITY OF CARE AFTER RELEASE

Management of chronic medical diseases, including chronic hepatitis B and its sequelae, should be bridged over to community healthcare settings after discharge from correctional facilities. In the setting of HIV infection, lack of continuity of care results in loss of viral control, presumably associated with lack of access to antiviral medications or relapse to drug use.[77] Timely initiation of discharge planning ensures continuity of care without any interruption and should include referral to medical care for continued access to discharge medications and immunizations, transitional housing, referrals to risk-reduction programs, and social services required to continue behavioral therapy. In addition, coordination and case management of long-term specialized care should be arranged for patients with disabling conditions, e.g. cirrhosis or HCC. Health education is of crucial significance for persons with blood-borne viral infections like HBV. These individuals should be educated about the risk factors for transmission of HBV, needle exchange programs, condom use, and avoidance of sharing toothbrushes, razors, etc. Vaccination of contacts should be arranged before patient discharge.

PUBLIC HEALTH IMPORTANCE OF DIAGNOSIS, PREVENTION, AND TREATMENT IN PRISONS

Correctional settings, with their structured environment and managed care approach, are ideal settings to screen, evaluate, and provide treatment and promote risk reduction interventions that will contribute to society's improved public health. The rationale for testing for HBV infection is multifold. First, correctional institutions have high prevalence of HBV infection, which can be effectively treated with newer therapies.[47] Second, undetected HBV has been associated with several outbreaks of acute HBV infection within correctional facilities that can be potentially avoided if HBV is detected upon entry.[16] Third, given the high rates of recidivism in this population, they impose a high risk of transmission of blood-borne pathogens, including HBV, after release to the community. Fourth, individuals who learn that they are infected with a chronic infection tend to reduce their risk behaviors by more than 50%, as has been shown for intravenous drug users with hepatitis C.[78] Fifth, a large percentage of prisoners are not immune to HBV and therefore eligible for vaccination consistent with existing public health guidelines.[35] Sixth, vaccination of prisoners has been demonstrated to be a cost-effective strategy, with savings of US$ 2.13 for each US$ 1 invested in vaccinating inmates.[79]

Cost–benefit has been demonstrated not only in the prevention by vaccination but also in diagnosis and treatment of the hepatic disease imposed by HBV infection. Management of chronic HBV disease can result in person-life-years saved, quality-of-life-improvement, as well as economic benefit. Treatment with lamivudine has been shown to be extremely cost-effective, although current cumulative evidence suggests high risk of resistance and low anticipation for virological cure with

lamivudine monotherapy and other agents are therefore preferred.[80] Cost–benefit analysis on newer anti-HBV agents can be anticipated once investigations of prolonged use in longitudinal studies have been completed. The direct medical costs alone incurred by HBV infection demand an escalating dollar amount investment with advancing stages of disease. Cost–benefit analyses have determined that diagnosis and treatment of chronic hepatitis B is far more beneficial than managing late sequelae of untreated HBV infection.[81] The annual healthcare cost of medical care for compensated cirrhosis increases more than 50-fold once hepatic decompensation occurs. Similarly, economic burden multiplies with diagnosis and management of HCC. Hepatic transplantation and post-transplant management impose the highest cost on the overall management of chronic hepatitis B.[81] From the societal perspective, taking into account the direct nonmedical costs and indirect costs (e.g., decreased productivity, increased dependence on ancillary support, increased mortality) would altogether increase the adverse impact several fold more. The cost-effectiveness of early diagnosis and treatment per quality adjusted life year of HBV infection is especially relevant in managed care setting with limited budgets, like correctional facilities, especially for HBV-infected individuals who are incarcerated for several years. Public health importance of diagnosis, vaccination, and treatment considerations cannot be overemphasized, however, even for inmates incarcerated for a few years, given the high-risk behavior in this population and potential for transmission to the community after release from correctional facilities.

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REFERENCES

1. Bureau of Justice Statistics, US Department of Justice. Bureau of Justice Statistics, 2006. Available at: http://www.ojp.usdoj.gov/bjs/prisons.htm. Accessed Dec 21, 2007.
2. Harrison PM, Beck AJ. *Prisoners in 2005*. Washington DC: US Department of Justice, Bureau of Justice Statistics; 2006.
3. Hammett TM, Harmon MP, Rhodes W. The burden of infectious disease among inmates of and releasees from US correctional facilities, 1997. *Am J Public Health*. 2002;92: 1789–1794.
4. Altice FL, Marinovich MA, Khoshnood K, Blankenship K, Springer S, Selwyn P. Correlates of HIV Infection Among Incarcerated Women. *J Urban Health*. 2005. 82 (2):312–326 doi:10.1093/jurban/jti055.
5. Health Status of Soon-to-be-Released Inmates. A Report to Congress, vol. 2. Washington, DC: National Commission on Correctional Health Care; 2002.
6. Conklin TJ, Lincoln T, Flanigan TP. A public health model to connect correctional health care with communities. *Am J Public Health*. 1998;88(8):1249–1250.
7. Altice FL, Springer SA. In: Mayer K, Pfizer HF, eds. *Management of HIV/AIDS in Correctional Settings The AIDS Pandemic: Impact on Science and Society*. San Diego, CA: Elsevier; 2005.
8. World Health Organization (WHO). *Wkly Epidemiol Rec* 79(28):253–264; 2004.
9. McQuillan GM, Coleman PJ, Kruszon-Moran D, Moyer LA, Lambert SB, Margolis HS. Prevalence of hepatitis B virus infection in the United States: the National Health and Nutrition Examination Surveys, 1976 through 1994. *Am J Public Health*. 1999;89:14–18.

10. CDC. US disease burden data 1980–2006. Available at: http://www.cdc.gov/ncidod/diseases/hepatitis/resource/index.htm#surveillance. Accessed on Oct 30, 2007.
11. Khan A, Goldstein S, Williams I, Bell B, Mast E. Opportunities for hepatitis B prevention in correctional facilities and sexually transmitted disease treatment settings. *Antivir Ther*. 2000;5(suppl 1):22.
12. Goldstein ST, Alter MJ, Williams IT, et al. Incidence and risk factors for acute hepatitis B in the United States, 1982–1998: implications for vaccination programs. *J Infect Dis*. 2002. 185:713–719 doi:10.1086/339192.
13. Hull HF, Lyons LH, Mann JM, Hadler SC, Steece R, Skeels MR. Incidence of hepatitis B in the penitentiary of New Mexico. *Am J Public Health*. 1985;75:1213–1214.
14. Centers for Disease Control and Prevention. Transmission of hepatitis B virus in correctional facilities–Georgia, January 1999-June 2002. *MMWR Morb Mortal Wkly Rep*. 2004;53(30):678–681.
15. Centers for Disease Control and Prevention. Hepatitis B outbreak in a state correctional facility, 2000. *MMWR Morb Mortal Wkly Rep*. 2001;50(25):529–532.
16. Khan A, Simard E, Wurtzel H, et al. The prevalence, risk factors, and incidence of hepatitis B virus infection among inmates in a state correctional facility [Abstract]. In: Program and abstracts of the 130th Annual Meeting of the American Public Health Association, Philadelphia, Pennsylvania, 2002.
17. Ruiz JD, Mikanda J. Seroprevalence of HIV, hepatitis B, hepatitis C, and risk behaviors among inmates entering the California Correctional System. California Department of Health Services, Office of AIDS, HIV/AIDS Epidemiology Office, March 1996.
18. Mikl J, Dzierbicki A, Smith PF, Greifinger R, Wright L, Morse DL. Trends in HIV infection rates among New York State (NYS) Prison Inmates, 1987–97. Poster abstract no. 23516 presented at 12th World AIDS Congress, June 30, 1998, Geneva, Switzerland.
19. Weinbaum C, Lyerla R, Margolis HS. Prevention and control of infections with hepatitis viruses in correctional settings. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2003;52(RR-1):1–36.
20. Macalino GE, Salas CM, Towe CW, et al. Incidence and community prevalence of HIV and other blood borne pathogens among incarcerated women in Rhode Island [Abstract]. Presented at the National HIV Prevention Conference. Atlanta, GA: US Department of Health and Human Services, CDC; 1999.
21. Charuvastra A, Stein J, Schwartzapfel B, et al. Hepatitis B vaccination practices in state and federal prisons. *Public Health Rep*. 2001;116:203–209.
22. McMahon BJ, Alward WL, Hall DB, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis*. 1985;151:599–603.
23. Iloeje UH, Yang HI, Su J. HBV viral load less than 104 copies/mL is associated with significant risk of hepatocellular carcinoma in chronic hepatitis B (CHB) patients: an update from the R.E.V.E.A.L.-HBV Study. In: Program and abstracts of the 58th Annual Meeting of the American Association for the Study of Liver Diseases; November 2–6, 2007; Boston, MA. Abstract 907.
24. Chu CJ, Keeffe EB, Han SH, et al. Hepatitis B virus genotypes in the United States: results of a nationwide study. *Gastroenterology*. 2003. 125(2):444–451 doi:10.1016/S0016-5085(03)00895-3.
25. Chan HL, Hui AY, Wong ML, Tse AML, Hung LCT, Sung JJY. Genotype C hepatitis B virus infection is associated with an increased risk of hepatocellular carcinoma. *Gut*. 2004. 53:1494–1498 doi:10.1136/gut.2003.033324.
26. Chu CJ, Hussain M, Lok AS. Hepatitis B virus genotype B is associated with earlier HBeAg seroconversion compared with hepatitis B virus genotype C. *Gastroenterology*. 2002. 122:1756–1762 doi:10.1053/gast.2002.33588.
27. Janssen HL, van Zonneveld M, Senturk H, et al. Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. *Lancet*. 2005. 365:123–129 doi:10.1016/S0140-6736(05)17701-0.

28. Di Marco V, Lo Iacono O, Camma C, et al. The long-term course of chronic hepatitis B. *Hepatology*. 1999. 30:257–264 doi:10.1002/hep.510300109.
29. Fattovich G, Giustina G, Schalm SW, et al. Occurrence of hepatocellular carcinoma and decompensation in western European patients with cirrhosis type B. The EUROHEP Study Group on Hepatitis B Virus and Cirrhosis. *Hepatology*. 1995;21: 77–82.
30. Yang HI, Lu SN, Liaw YF, et al. Hepatitis B e antigen and the risk of hepatocellular carcinoma. *N Engl J Med*. 2002. 347:168–174 doi:10.1056/NEJMoa013215.
31. Chen CJ, Yang HI, Su J, et al. Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DNA level. *JAMA*. 2006. 295(1):65–73 doi:10.1001/jama.295.1.65.
32. Iloeje UH, Yang HI, Su J, Jen CL, You SL, Chen CJ, et al. Predicting cirrhosis risk based on the level of circulating hepatitis B viral load. *Gastroenterology*. 2006. 130:678–686 doi:10.1053/j.gastro.2005.11.016.
33. Ahn SH, Han KH, Park JY, et al. Association between hepatitis B virus infection and HLA-DR type in Korea. *Hepatology*. 2000. 31(6):1371–1373 doi:10.1053/jhep.2000.7988.
34. Chu RH, Ma LX, Wang G, Shao LH. Influence of HLA-DRB1 alleles and HBV genotypes on interferon-alpha therapy for chronic hepatitis B. *World J Gastroenterol*. 2005;11 (30):4753–4757.
35. Centers for Disease Control and Prevention. Notice to readers update recommendations to prevent hepatitis B virus transmission—United States. *MMWR Morb Mortal Wkly Rep*. 1999;48(2):33–34.
36. Centers for Disease Control and Prevention. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep*. 1991;40(RR-13):1–25.
37. Charuvastra A, Stein J, Schwartzapfel B, et al. Hepatitis B vaccination practices in state and federal prisons. *Public Health Rep*. 2001;116:203–209.
38. Bick JA. Infection control in jails and prisons. *Clin Infect Dis*. 2007. 45:1047–1055 doi:10.1086/521910.
39. Bond WW, Favero MS, Petersen NJ, Gravelle CR, Ebert JW, Maynard JE. Survival of hepatitis B virus after drying and storage for one week. *Lancet*. 1981. 1(8219):550–551 doi:10.1016/S0140-6736(81)92877-4.
40. Petersen NJ, Barrett DH, Bond WW, et al. Hepatitis B surface antigen in saliva, impetiginous lesions, and the environment in two remote Alaskan villages. *Appl Environ Microbiol*. 1976;32(4):572–574.
41. Mast EE, Weinbaum CM, Fiore AE, et al. 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*. 2006;55(RR-16):1–33.
42. Fonseca MO, Pang LW, de Paula Cavalheiro N, Barone AA, Heloisa Lopes M. Randomized trial of recombinant hepatitis B vaccine in HIV-infected adult patients comparing a standard dose to a double dose. *Vaccine*. 2005. 23:2902–2908 doi:10.1016/j.vaccine.2004.11.057.
43. Wright NM, Campbell TL, Tompkins CN. Comparison of conventional and accelerated hepatitis B immunisation schedules for homeless drug users. *Commun Dis Public Health*. 2002;5:324–326.
44. Altice FL, Bruce RD, Walton MR, Buitrago MI. Adherence to hepatitis B virus vaccination at syringe exchange sites. *J Urban Health*. 2005. 82(1):151–161 doi:10.1093/jurban/jti016.
45. Lok AS, McMahon J. AASLD practice guidelines for chronic hepatitis B. *Hepatology*. 2007. 45(2):507–539 doi:10.1002/hep.21513.

46. Keeffe EB, Dieterich DT, Han SB, et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: an update. *Clin Gastroenterol Hepatol*. 2006. 4:936–962 doi:10.1016/j.cgh.2006.05.016.
47. Gish RG. Improving outcomes for patients with chronic hepatitis B. *Curr Gastroenterol Rep*. 2007. 9(1):14–22 doi:10.1007/s11894-008-0016-9.
48. Chang TT, Gish GR, de Man R, et al. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis. *N Engl J Med*. 2006. 354:1001–1010 doi:10.1056/NEJMoa051285.
49. Marcellin P, Buti M, Krastev Z, et al. A randomized, double-blind, comparison of tenofovir DF (TDF) versus adefovir dipivoxil (ADV) for the treatment of HBeAg-negative chronic hepatitis B (CHB): study GS-US-174-0102. In: Program and abstracts of the 58th Annual Meeting of the American Association for the Study of Liver Diseases; November 2–6, 2007; Boston, Massachusetts. Abstract LB2.
50. Buti M, Hadziyannis S, Mathurin P. Tenofovir Disoproxil Fumarate (TDF) is Highly Active for Treatment of Chronic Hepatitis B (CHB) in Patients With Cirrhosis. Abstract presented at 43rd Annual Meeting of the European Association for the Study of the Liver; April 23–27, 2008; Milan, Italy
51. Heathcote E, Gane E, DeMan R, et al. A randomized, double-blind, comparison of tenofovir DF (TDF) versus adefovir dipivoxil (ADV) for the treatment of HBeAg positive chronic hepatitis B (CHB): study GS-US-174-0103. Program and abstracts of the 58th Annual Meeting of the American Association for the Study of Liver Diseases; November 2–6, 2007; Boston, MA. Abstract LB6.
52. Gish R, Chang TT, Lai CL, et al. Hepatitis B surface antigen loss in antiviral-treated patients with HBeAg-positive chronic hepatitis B infection: observations from antiviral-naive patients treated with entecavir or lamivudine. *Hepatology*. 2006;44:558A.
53. Korevaar A, Moucari R, Asselah T, et al. High rates of HBsAg seroconversion in chronic hepatitis B patients responding to interferon therapy: a long-term follow-up study. In: Program and abstracts of the 58th Annual Meeting of the American Association for the Study of Liver Diseases; November 2–6, 2007; Boston.
54. Keeffe EB, Zeuzem S, Koff RS, et al. Report of an international workshop: roadmap for management of patients receiving oral therapy for chronic hepatitis B. *Clin Gastroenterol Hepatol*. 2007. 5:890–897 doi:10.1016/j.cgh.2007.05.004.
55. Lok AS, Lai CL, Leung N, et al. Long-term safety of lamivudine treatment in patients with chronic hepatitis B. *Gastroenterology*. 2003. 125:1714–1722 doi:10.1053/j.gastro.2003.09.033.
56. Benhamou Y, Bochet M, Thibault V, et al. Long-term incidence of hepatitis B virus resistance to lamivudine in human immunodeficiency virus-infected patients. *Hepatology*. 1999. 30:1302–1306 doi:10.1002/hep.510300525.
57. Marcellin P, Chang TT, Lim SG, et al. Long-term efficacy and safety of adefovir dipivoxil (ADV) in HBeAg+ chronic hepatitis B patients: increasing serologic, virologic, and biochemical response over time. *Hepatology*. 2004. 40(Suppl 1):665A doi:10.1002/hep.20257.
58. Hadziyannis SJ, Tassopoulos NC, Heathcote EJ, et al. Long-term therapy with adefovir dipivoxil for HBeAg-negative chronic hepatitis B. *N Engl J Med*. 2005. 352:2673–2681 doi:10.1056/NEJMoa042957.
59. Lai CL, Gane E, Hsu CW, et al. Two-year results from the GLOBE trial in patients with hepatitis B: greater clinical and antiviral efficacy for telbivudine (LdT) vs. lamivudine. *Hepatology*. 2006;44(4):222A.
60. van Bommel F, Mauss S, Schurmann D, et al. No evidence for tenofovir resistance in patients with lamivudine-resistant HBV infection during long-term treatment for up to 5 years. *Hepatology*. 2006. 44(Suppl):A549 (abstract)doi:10.1002/hep.21253.
61. Lee HS, Chung YH, Lee KS, et al. A 12-week clevudine therapy showed potent and durable antiviral activity in HBeAg-positive chronic hepatitis B. *Hepatology*. 2006. 43:982–988 doi:10.1002/hep.21166.

62. Han S, Chang TT, Chao YC, et al. Four-year entecavir treatment in nucleoside-naive HbeAg+ patients: results from studies ETV-022 and -901. *Hepatology*. 2007;46:654A.
63. Manns M, Jeffers L, Dalekos G. The antiviral response to tenofovir is comparable in lamivudine (LAM)-naïve and LAM-experienced subjects treated for chronic hepatitis B (CHB). Abstract presented at 43rd Annual Meeting of the European Association for the Study of the Liver; April 23-27, 2008; Milan, Italy
64. van Bömmel F, De Man RA, Petersen J. A Multicenter analysis of antiviral response to tenofovir in HBV mono-infected patients with prior nucleos(t)ide analogue experience. Abstract presented at 43rd Annual Meeting of the European Association for the Study of the Liver; April 23–27, 2008; Milan, Italy.
65. Berg T, Moller B, Trinh H. Tenofovir (TDF) Versus emtricitabine plus TDF for treatment of chronic hepatitis B in subjects with persistent viral replication receiving adefovir dipivoxil (ADV). Abstract presented at 43rd Annual Meeting of the European Association for the Study of the Liver; April 23–27, 2008; Milan, Italy
66. Hui CK, Zhang HY, Bowden S, et al. 96 weeks combination of adefovir dipivoxil plus emtricitabine versus adefovir dipivoxil monotherapy in the treatment of chronic hepatitis B. *J Hepatol*. 2008. 48(5):714–720 doi:10.1016/j.jhep.2007.10.013.
67. Sung JJY, Lai JY, Zeuzem S, et al. Lamivudine compared with lamivudine and adefovir dipivoxil for the treatment of HBeAg-positive chronic hepatitis B. *J Hepatol*. 2008. 48 (5):725–735 doi:10.1016/j.jhep.2007.12.026.
68. Xu WM, Cui YT, Wang L, et al. Efficacy and safety of lamivudine in late pregnancy for the prevention of mother-child transmission of hepatitis B: a multicenter, randomised, double-blind, placebo-controlled study (abstr). *Hepatology*. 2004;40:272A–273A.
69. Lee JS, Mullaney S, Bronson R, et al. Transplacental antiretroviral therapy with 9-(2-phosphonylmethoxyethyl)adenine is embryotoxic in transgenic mice. *J Acquir Immune Defic Syndr*. 1991. 4(9):833–838 doi:10.1097/00126334-199109000-00001.
70. Thio CL, Seaberg EC, Skolasky R Jr, et al. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter AIDS Cohort Study (MACS). *Lancet*. 2002. 360:1921–1926 doi:10.1016/S0140-6736(02)11913-1.
71. Bodsworth N, Donovan B, Nightingale BN. The effect of concurrent human immunodeficiency virus infection on chronic hepatitis B: a study of 150 homosexual men. *J Infect Dis*. 1989;160(4):577–582.
72. Guidelines for Use of Antiretroviral Agents in HIV-1 infected adults and adolescents. Available at: http://aidsinfo.nih.gov/Guidelines. Accessed on Jan. 2008.
73. McMahon M, Jilek B, Brennan T, et al. The anti-hepatitis B drug entecavir inhibits HIV-1 replication and selects HIV-1 variants resistant to antiretroviral drugs. Abstract presented at the 14th Conference on Retroviruses and Opportunistic Infections, Los Angeles, CA, February 2007.
74. Lin L, Verslype C, van Pelt JF, van Ranst M, Fevery J. Viral interaction and clinical implications of coinfection of hepatitis C virus with other hepatitis viruses. *Eur J Gastroenterol Hepatol*. 2006. 18(12):1311–1319 (review)doi:10.1097/01.meg.0000243881.09820.09.
75. Saitta C, Pontisso P, Brunetto MR, et al. Virological profiles in hepatitis B virus/hepatitis C virus coinfected patients under interferon plus ribavirin therapy. *Antivir Ther*. 2006;11 (7):931–934.
76. Bruix J, Sherman M. AASLD practice guidelines: management of hepatocellular carcinoma. *Hepatology*. 2005. 42(5):1208–1236 doi:10.1002/hep.20933.
77. Springer SA, Pesanti E, Hodges J, Macura T, Doros G, Altice FL. Effectiveness of antiretroviral therapy among HIV-infected prisoners: reincarceration and the lack of sustained benefit after release to the community. *Clin Infect Dis*. 2004. 38(12):1754–1760 doi:10.1086/421392.
78. Kwiatkowski CF, Fortuin Corsi K, Booth RE. The association between knowledge of hepatitis C virus status and risk behaviors in injection drug users. *Addiction*. 2002. 97 (10):1289–1294 doi:10.1046/j.1360-0443.2002.00208.x.

79. Pisu M, Meltzer MI, Lyerla R. Centers for Disease Control and Prevention (CDC). Cost-effectiveness of hepatitis B vaccination of prison inmates. *Vaccine*. 2002. 21(3–4):312–321 doi:10.1016/S0264-410X(02)00457-7.
80. Enriquez AD, Campbell MS, Reddy KR. Cost-effectiveness of suppressing hepatitis B virus DNA in immune tolerant patients to prevent hepatocellular carcinoma and cirrhosis. *Aliment Pharmacol Ther*. 2007;26:383–391.
81. Lee TA, Veenstra DL, Iloeje UH, Sullivan SD. Cost of chronic hepatitis B infection in the United States. *J Clin Gastroenterol*. 2004. 38:S144–S147 doi:10.1097/00004836-200411003-00005.