

A *prn* PRIMARY CARE ALGORITHM HEPATITIS B AND HIV COINFECTION

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Dr. James F. Braun,
Editor-in-Chief
Meri D. Pozo, PhD,
Managing Editor
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Executive Director
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Initial HBV Screening				
HBsAg	Anti-HBs	Anti-HBc	Anti-HBc (IgM)	
-	-	-	-	Needs HBV vaccine
-	+	-	-	Established immunity (vaccinated)
-	+	+	-	Latent or prior infection
-	-	+	-	Usually either latent infection or false positive. Small percentage may reflect active infection; HBV-DNA follow-up testing recommended (only immune-compromised patients). Consider vaccination if false positive.
+	-	+	+	Acute HBV infection
+	-	+	-	Chronic infection

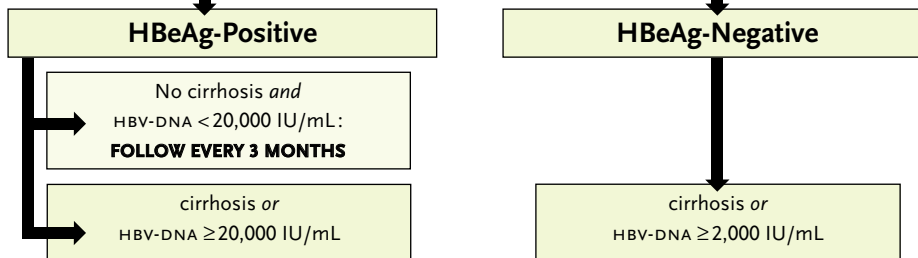
Baselines

- Screen for HIV, HCV, HDV and HAV
 - Vaccinate against HAV if not immune
- ALT and AFP
- HBeAg, Anti-HBe and HBV-DNA

Follow-Up HBV Laboratory Interpretation			
HBsAg	Anti-HBe	HBV-DNA*	
-	+	<2,000 IU/mL	Lower level replication (Rescreen HBV-DNA every 6 months or if ALT increases)
+	-	≥2,000 IU/mL	Chronic infection with viral replication — HBeAg-positive disease
-	+/-	≥2,000 IU/mL	Chronic infection with viral replication — HBeAg-negative disease ("precore mutant")

Further Work-Up for Chronic HBV

- Referral to Hepatologist or ID specialist annually
- If HIV+ with current or prior ARV experience screen for HBV drug resistance
- Hepatic Imaging
 - MRI or quadruple-phase helical CT (preferable if available) or
 - Ultrasound with AFP (every 6 to 12 months)
 - If hepatoma suspected, refer to Oncologist
- Consider baseline liver biopsy



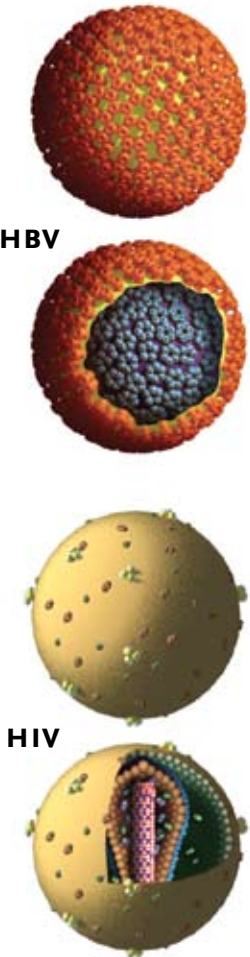
TREATMENT

HBeAg-positive: Treat until 6 to 12 months after anti-HBe seroconversion. If on ART, treat long term.

HBeAg-negative (precore mutant): Long-term treatment for viral suppression necessary

Many people with HIV disease also have chronic hepatitis B, and vice versa. It is extremely important to screen for coinfection in either case. This algorithm was developed by the editorial faculty of *The prn Notebook* to illustrate the various steps involved in the screening, diagnosis, and clinical care of patients with chronic HBV infection. *prn* does not seek to make any recommendations, per se, but rather to define the current standard of medical care — and the evolving options — for both HBV-monoinfected and HBV/HIV-coinfected patients. Expert clinicians involved in the development of this algorithm are:

- Kevin Armington, MD
- James F. Braun, DO
- Mark Danta, MD
- Douglas T. Dieterich, MD
- Geoffrey Dusheiko, FCP(SA), FRCP, FRCP(Edin)
- Daniel Fierer, MD
- Oren Fix, MD, MSc
- Edward Goldberg, MD
- Stephen Locarnini, BSc(Hons), MBBS, PhD, FRC(Path)
- Marion Peters, MD
- Anita Radix, MD
- Joe Sasadeusz, MBBS, FRACP, PhD
- Hans Tillmann, MD
- Karen Weisz, CFNP



HIV/HBV-Coinfected Patients	
HIV TREATMENT NOT YET INDICATED	HIV TREATMENT INDICATED
<p>Do NOT use any HBV drug which will select for resistance to HIV. In accordance with DHHS Guidelines, therapeutic options for HIV/HBV-coinfected patients who do not yet require a tenofovir-, lamivudine-, or emtricitabine-containing antiretroviral drug regimen:</p> <p>Adefovir dipivoxil (Hepsera®) (10 mg QD)[†]</p> <ul style="list-style-type: none"> • Dose too low to confer activity against HIV; unlikely risk of HIV cross-resistance to tenofovir. • Effective for the treatment of HBV in coinfecting patients, including lamivudine-resistant HBV. • HBV resistance develops in 18% after 4 years and in 29% after 5 years. • May consider using in combination with either entecavir or telbivudine to reduce the risk of HBV resistance. However, a recent report suggests that entecavir might have some anti-HIV activity leading to HIV drug resistance in coinfecting individuals. <p>Entecavir (Baraclude®) (0.5 mg QD or 1 mg QD)[†]</p> <ul style="list-style-type: none"> • Caution: a recent report suggests that ETV might have some anti-HIV activity leading to HIV drug resistance. • Limited HBV resistance with prolonged monotherapy, but only 3 years of follow-up data thus far. • ETV resistance has been noted in patients with pre-existing YMDD mutations, reaching 30% at 3 years of therapy. • May consider combination therapy with adefovir to reduce the risk of HBV drug resistance. <p>Peginterferon alfa-2a (Pegasys®) (180 µg SC QW x 48 weeks)[†]</p> <ul style="list-style-type: none"> • More effective than conventional interferon for treating HBeAg-positive HBV infection. • Greater sustained suppression after therapy completion compared to lamivudine monotherapy in HBeAg-positive and HBeAg-negative disease; addition of lamivudine to peginterferon alfa-2a did not improve response rates. • Not specifically approved for HIV/HBV coinfection. • May not be as effective in coinfecting patients; likely most effective in patients with CD4+ counts >350 cells/mm³. • HBV genotypes A and B respond better to interferon than HBV genotypes C and D; pretreatment genotyping recommended. • Preferred treatment for chronic HBV with HDV superinfection. <p>Telbivudine (Tyzeka®) (600 mg QD)[†]</p> <ul style="list-style-type: none"> • No known anti-HIV activity. • Effective in HBeAg-positive and HBeAg-negative patients. • Significantly lower risk of resistance than lamivudine. • May consider using in combination with adefovir to reduce risk of HBV resistance. 	<p>In accordance with 2006 DHHS Guidelines, therapy should be initiated with a regimen containing tenofovir plus lamivudine or emtricitabine in HIV/HBV-coinfected patients requiring antiretroviral treatment. Clinicians should closely monitor LFTs, especially when using drugs associated with hepatotoxicity in the setting of chronic HBV infection (e.g., nevirapine). When initiating or changing HIV treatment, use 2 active anti-HBV agents and at least 3 anti-HIV agents. HIV ART that includes tenofovir, lamivudine or emtricitabine should not be abruptly discontinued due to the risk of severe hepatic flares.</p> <p>Also be aware of and monitor for Immune Restoration Disease (IRD), which is a phenomenon where improved immune function following initiation of HAART, especially in those with a low CD4 count, can induce severe HBV flares. Such flares can occur within weeks after starting HAART, even when anti-HBV agents are included in the HAART regimen, as there is insufficient time for reduction of HBV DNA. Patients with advanced fibrosis may be even more vulnerable to this life-threatening phenomenon. In advanced disease, pre-treatment to control HBV with an agent that does not have anti-HIV activity may be advisable before initiating HAART containing anti-HBV components.</p> <p>Emtricitabine (Emtriva®) (200 mg QD)[†]</p> <ul style="list-style-type: none"> • Not FDA approved for the treatment of HBV. • Preliminary data indicate activity against HBV; HBV drug resistance pattern is similar to lamivudine. • Coformulated with tenofovir (Truvada®). <p>Lamivudine (Epivir®) (150 mg BID or 300 mg QD)[†]</p> <ul style="list-style-type: none"> • Use dose indicated for HIV infection. • HBV resistance develops in 25% of patients after 1 year and in 90% after 4 years. <p>Tenofovir (Viread®) (300 mg QD)[†]</p> <ul style="list-style-type: none"> • Not FDA approved for the treatment of HBV, but is preferred over Adefovir in HBV/HIV when HIV treatment is indicated, in combination with lamivudine or emtricitabine as components of HAART. • Limited data in HIV/HBV-coinfected patients; preliminary data suggest superior anti-HBV activity compared to adefovir. • Coformulated with emtricitabine (Truvada®). <p>Entecavir (Baraclude®) (0.5 mg QD or 1 mg QD)[†]</p> <ul style="list-style-type: none"> • Effective for the treatment of HBV in coinfecting patients, including lamivudine-resistant HBV. • Dose dependent on previous nucleoside analogue experience. • ETV resistance has been noted in patients with pre-existing YMDD mutations, reaching 30% at 3 years of therapy. • A recent report suggests that ETV, when given as monotherapy for HBV in HIV coinfecting patients, might have some anti-HIV activity leading to HIV drug resistance, but this has not been reported when ETV is coadministered with combination ART. <p>Peginterferon alfa-2a (Pegasys®) (180 µg SC QW x 48 weeks)[†]</p> <ul style="list-style-type: none"> • See Left Column.

HBV-Monoinfected Patients (verify HIV negative status)
<p>Adefovir dipivoxil (Hepsera®) (10 mg QD)[†]</p> <ul style="list-style-type: none"> • Safe and effective anti-HBV treatment, including lamivudine-resistant HBV. • Use alone or in combination with lamivudine for cirrhotic patients. • HBV resistance develops in 18% after 4 years and in 29% after 5 years. • May consider combination therapy with entecavir or telbivudine to reduce risk of resistance. <p>Entecavir (Baraclude®) (0.5 mg QD or 1 mg QD)[†]</p> <ul style="list-style-type: none"> • Dose dependent on previous nucleoside analogue experience. • Superior to lamivudine as first-line therapy. • Effective against lamivudine-refractory HBV using 1 mg QD dose. • Limited HBV resistance with prolonged monotherapy, but only 3 years of follow-up data thus far. • ETV resistance has been noted in patients with preexisting YMDD mutations, reaching 30% at 3 years of therapy. <p>Lamivudine (Epivir-HBV®) (100 mg QD)[†]</p> <ul style="list-style-type: none"> • Safe and effective anti-HBV treatment but limited by the development of rapid HBV resistance. • HBV resistance (as monotherapy) develops in 15% to 32% of patients in 1 year and in 67% after four years. <p>Peginterferon alfa-2a (Pegasys®) (180 µg SC QW x 48 weeks)[†]</p> <ul style="list-style-type: none"> • More effective than conventional interferon for treating HBeAg-positive HBV infection. • Greater sustained suppression after therapy completion compared to lamivudine monotherapy in HBeAg-positive and HBeAg-negative disease; addition of lamivudine to peginterferon alfa-2a did not improve response rates. • HBV genotypes A and B respond better to interferon than HBV genotypes C and D; pretreatment genotyping recommended. • Preferred treatment for chronic HBV with HDV superinfection. <p>Telbivudine (Tyzeka®) (600 mg QD)[†]</p> <ul style="list-style-type: none"> • More effective than lamivudine. • Effective in HBeAg-positive and HBeAg-negative patients. • Significantly lower risk of HBV resistance than lamivudine. • May consider combination therapy with adefovir to reduce the risk of HBV drug resistance.

ANTI-HBV AGENTS IN DEVELOPMENT
<p>Pradefovir (Phase 2 data)</p> <ul style="list-style-type: none"> • 14-fold higher pMEA levels than adefovir. • 5.02-log HBV DNA reduction versus 3.66-log reduction with adefovir at week 24. <p>Clevudine (Phase 2 data, now entering Phase 3 trials)</p> <ul style="list-style-type: none"> • 5.10- and 4.25-log HBV DNA reduction at 24 weeks in HBeAg-positive and HBeAg-negative patients, respectively. • Durable response in a significant proportion of patients after stopping treatment at week 24.

* Conversion of HBV-DNA copies to International Units, the current laboratory standard, is assay dependant, approximately 5 copies/mL=1 IU/mL. Verify conversion factor with your reference laboratory. † Adjust for renal dysfunction