

MAT TRAINING

PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Hepatitis C and B Prevention and Treatment in Persons who Use Drugs

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Frances Levin, MD is a consultant for GW Pharmaceuticals and receives study medication from US Worldmed. This planning committee for this activity has determined that Dr. Levin's disclosure information poses no bias or conflict to this presentation.

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System Requirements

- In order to complete this online module you will need Adobe Reader. To install for free click the link below:
 - <http://get.adobe.com/reader/>

Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

Educational Objectives

- At the conclusion of this activity participants should be able to:
 - Understand the importance of HCV and HBV screening among persons who use drugs.
 - Understand the treatment options for HCV and HBV infected persons who use drugs.
 - Be aware of special issues related to treatment of HCV and HBV in those co-infected with HIV.

Outline

- Introduction
- Hepatitis C (HCV)
 - Epidemiology of HCV in Substance Using Persons
 - Screening & Prevention of HCV Infection
 - Current HCV Treatment Recommendations
 - Special Issues for HCV / HIV Co-Infected Persons
- Hepatitis B (HBV)
 - Epidemiology of HBV in Substance Using Persons
 - Screening & Prevention of HBV infection
 - Current HBV Treatment Recommendations
 - Special Issues for HBV/ HIV Co-Infected Persons
- Hepatitis A (HAV)

Introduction

- Viral Hepatitis is the leading infectious cause of death in the United States (U.S.) (\approx 12-15K /year).
- An estimated 3.5-5.3 million persons are living with viral hepatitis (mainly HCV and HBV) in the U.S.
- 65-75% of infected individuals in the U.S. remain unaware of their infection status and not in treatment.
- Viral hepatitis is the leading cause of liver transplantation in the U.S, and rates of liver cancer are rising (mainly due to HCV).
- Persons at higher risk for HCV in the U.S. are men who have sex with men (MSM) and persons who inject drugs (PWID).
- Costs of end-stage treatment of HCV and HBV infection (e.g. liver transplant) are on the rise as well but treatments for HCV and HBV can reduce morbidity and mortality and are cost-effective.
- Alcohol greatly exacerbates the progression to cirrhosis in HBV and HCV infection and thus abstinence from alcohol is recommended.

Hepatitis C (HCV)

Epidemiology of HCV Infection in Persons Who Use Drugs (PWID)

- \approx 150 million persons in the world have chronic HCV¹
- \approx 3.7 million persons in U.S. have chronic HCV¹
- 50-80% of HCV is among persons who actively (past <6 months) or formerly injected drugs (e.g. history of and/or on OST)²
- \approx 20K persons/year are newly infected with HCV in U.S.⁴
- \approx 50% of new HCV cases in U.S. are among PWID⁴
- 75% of all new HCV infection progresses to chronic infection
- 25% of all chronic HCV infections progress to cirrhosis and end-stage liver disease (ESLD) and/or hepatocellular carcinoma (HCC) over 20-30 years³; In PWID, 20-year cirrhosis prevalence is \approx 15%⁴

Persons in Whom HCV Testing is Recommended:

- Adults born during 1945-1965 should be tested once (without assessment of HCV risk factors)
- Current IDUs
- Persons who ever injected drugs
- Persons who ever received clotting factor concentrates before 1987
- Persons who were ever on long-term hemodialysis
- Persons with abnormal ALT levels
- Persons with HIV infection
- Persons who were prior recipients of transfusions or organ transplants including persons who:
 - Were notified that they received blood from a donor who later tested + for HCV
 - Received a transfusion of blood, blood components or an organ transplant before July 1992
- A recognized exposure (for those who may have been exposed in last 6 months, then test for HCV RNA plus HCV AB in follow-up too):
 - Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV+ blood
 - Children born to HCV+ women

Routine HCV testing is of Uncertain Need for the Following Groups:

- Recipients of transplanted tissue (e.g. corneal, musculoskeletal, skin, ova, sperm)
- Intranasal cocaine and other non-injecting illegal drug users
- Persons with a history of tattooing or body piercing
- Persons with a history of multiple sex partners or STDs
- Long-term steady sex partners of HCV+ persons

<http://www.cdc.gov/hepatitis/hcv/guidelinesc.htm>

Increasing Access to Hepatitis C Testing Among Persons Who Use Drugs (PWID)

- Assessment for HCV is low among persons who inject drugs
- Effectively engaging PWID in HCV care through HCV assessment and treatment, via HCV nursing and HCV specialist support in integrated opioid substitution treatment (OST) or community health clinics (CHCs) can increase engagement in HCV care (ETHOS study)¹

Screening for HCV Chronic Infection

- An initial visit with an HCV antibody (HCV Ab)^{1-2,4} is recommended for first screen
 - If negative, repeat every 6–12 months for those with ongoing risk behaviors (e.g. IDU, MSM) ³
 - If HCV AB is positive or if negative but suspect acute HCV infection then check HCV RNA level⁴
 - More frequent surveillance if ongoing risk occurs
- All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated given increase in progression to chronic liver disease with on-going alcohol use
- All persons found to have chronic HCV infection should be referred to appropriate care and treatment services for HCV infection and related conditions

Prevention of HCV Infection in PWID

- Behavioral interventions alone have not been effective at reducing spread of HCV; combinations of interventions are now recommended¹
- PWID should be provided with clean drug-injecting equipment and access to OST as part of widespread comprehensive harm reduction programs, including in prisons⁵
- Combination of opioid substitution treatment (OST) + needle & syringe exchange programs (NSEPs) result in large reductions in HCV transmission²
- Mathematical modeling of OST + NSEPs+ HCV treatment suggest large reductions (>45%) in HCV chronic prevalence over 10 years³
- HCV vaccine in development: early, possibly protective, immunity against persistent HCV is possible; trials on-going in PWID⁴

OST Among PWID as HCV Prevention

- Active drug use is a predictor of HCV treatment deferral¹ and of poor HCV treatment uptake²⁻⁵
- Buprenorphine & methadone (OSTs) are associated with lower HCV treatment deferral^{1,6}
- OST is effective at reducing HCV & HIV -risk behaviors and transmission⁷
- OST with NSEPs without HCV treatment may not substantially reduce HCV prevalence⁸, although they decrease drug related deaths and drug-related crime^{9,10}
- Mathematical modeling has shown that HCV treatment for active PWID could prevent further transmission and be more cost-effective than treating former PWID due to prevented secondary infections^{11,12}

1. Gidding et al., 2011; 2. Grebely et al., 2011; 3. Butt et al., 2007; 4. Mehta et al., 2008; 5. Rocca et al., 2004; 6. Grebely et al., 2009. Turner et al., 2011, 8. Vickerman et al., 2012; 9. Cornish et al., 2010; 10. Bukten et al., 2012; 11. Martin et al., 2011; 12. Martin et al., 2013 .

Goal of HCV treatment

- “The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by an sustained viral response (SVR)” (i.e. undetectable HCV RNA level at 12 weeks after finishing treatment course).
 - SVR is a marker for cure of HCV infection and has been shown to be durable in large prospective studies in more than 99% of patients followed up for 5 years or more.

Recommendations for when and in whom to initiate treatment (1)

- Treatment is assigned to the highest priority for those patients with:
 - Advanced fibrosis
 - Compensated cirrhosis
 - Liver transplant recipients
 - Severe extrahepatic Hepatitis C
 - e.g. essential mixed cryoglobulinemia with end-organ damage, proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

Recommendations for when and in whom to initiate treatment (2)

- High Priority for Treatment owing to High Risk for Complications:
 - Fibrosis (Metavir F2)
 - HIV-1 Co-infection
 - HBV Co-infection
 - Other liver disease (NASH)
 - Debilitating fatigue
 - Diabetes mellitus (insulin resistant)
 - Porphyria cutanea tarda

Recommendations for when and in whom to initiate treatment (3)

- Persons whose Risk of HCV Transmission is High and in whom HCV Treatment may yield Transmission Reduction Benefits:
 - MSM with high-risk sexual practices
 - Active injection drug users
 - Incarcerated persons
 - Persons on long-term hemodialysis

Enhancing HCV Treatment in Persons who Actively Use Drugs

- HCV can be treated in active PWID¹
 - most studies use combinations of former and active drug users with few data on HCV treatment outcomes among active PWID alone.
- A systematic review and meta-analysis of treatment for HCV among active PWID found an overall SVR of 56%²
 - Although a lower SVR than some reports, it is the first systematic review among active PWID and illustrates that active PWID can respond favorably to HCV antiviral therapy

Enhancing HCV Treatment in Persons who Actively Use Drugs (2)

- Directly observed therapy (DOT) of Peg-Interferon + Ribavirin for HCV among active PWID lead to a higher proportion of patients with SVR as compared to those who delayed HCV treatment¹
- Psychoeducation among active PWID receiving OST may enhance adherence to HCV treatment and reduce dropouts²

Managing HCV Treatment Among PWID

- Previous HCV treatment guidelines excluded PWID from consideration of HCV treatment due to concerns for adherence, side effect susceptibility, reinfection, possible drug interactions with HIV ART
- Newer recommendations include active PWID³
 - The reinfection rate of HCV among PWID is actually low (1-5% per year)¹
 - Newer oral agents to treat Hepatitis C cause fewer side effects than interferon-based regimens
 - HIV & HCV antiviral regimen drug-drug interactions are now well known^{2,3}

Current HCV FDA-approved Treatment Options

- Pegylated Interferon (Peg-INF) injection once weekly + weight based oral Ribavirin (RBV) twice daily
- HCV Ns3/4A serine protease inhibitors, Direct acting antiviral, (DAAs) oral agents, with Peg INF + RBV: sustained virologic response (SVR) of 62-74%^{1,2}
 - Boceprevir (Victelis, Merck, 2011)
 - Telaprevir (Incivek, Vertex, 2011)
 - Simeprevir (Olysio, Janssen, 2013) approved with Peg-INF +RBV for GT¹
- NS5B-RNA-dependent RNA Polymerase Inhibitor
 - Sofosbuvir (Sovaldi, Gilead): 400 mg oral once daily with oral Ribavirin weight based twice daily³
 - Genotype (GT) 1 or 4: + Peg INF + RBV for 12 weeks; GT 2 : RBV for 12 weeks; GT 3: + RBV for 24 weeks
 - Sofosbuvir + Ribavirin for GT 1 for 24 weeks⁵ also has evidence a
 - Sofosbuvir + Simeprevir , can be used in GT 1 patients for 12 weeks

Recommended Initial Starting Regimens for HCV infection (GT1)

- **GT 1: Treatment-Naïve and eligible to receive IFN:**
 - Daily Sofosbuvir 400mg + Ribavirin (RBV) weight based + weekly PEG INF for 12 weeks
- **GT 1: Treatment-Naïve and NOT eligible to receive IFN:**
 - Daily Sofosbuvir 400mg + Simeprevir (150mg) with or without weight based RBV for 12 weeks
- **GT 1: Treatment-Naïve eligible to receive IFN. Alternative regimen:**
 - Daily Simeprevir 150mg x 12 weeks + Weight based RBV + weight-based PEG INF for 24 weeks

Not recommended for HCV GT 1 Infection

- PEG IFN + RBV + Telaprevir or Boceprevir is no longer a recommended regimen for GT 1-Naïve patients
- This is due to fact that they have been found to be inferior to Sofosbuvir and simeprevir, with increased side effects, high pill burden, many drug-drug interactions

HCV Starting Treatment recommendations (GT 2-6)

- **GT 2: Treatment-Naïve, regardless of IFN eligibility:**
 - Daily Sofosbuvir (400mg) + Weight-based RBV for 12 weeks
- **GT 3: Treatment-Naïve, regardless of IFN eligibility:**
 - Daily Sofosbuvir (400mg) + Wt-based RBV for 24 weeks
 - Daily Sofosbuvir (400mg) + Wt-based RBV + weekly PEG IFN for 12 weeks
- **GT 4: Treatment-Naïve, eligible to receive IFN:**
 - Daily Sofosbuvir (400mg) + Wt-based RBV + weekly PEG IFN x 12 weeks
 - Daily simeprevir (150mg) for 12 weeks + Wt Based RBV + weekly PEG IFN for 24-48 weeks.
- **GT 4: Treatment-Naïve, Not eligible to receive IFN:**
 - Daily Sofosbuvir (400mg) + Wt-based RBV for 24 wks
- **GT 5/6: Treatment-Naïve:**
 - Daily Sofosbuvir (400mg) + Wt-based RBV + weekly PEG IFN for 12 weeks
 - Daily Weight-based RBV + Weekly PEG IFN for 48 weeks

Treatment of HCV in HIV and HCV Co-Infected Patients

- 80% of patients with HIV also have HCV
- The DDAS (Telaprevir (TVP), Boceprevir (BCP) and Simeprevir) + Peg-INF + RBV are effective for HCV in co-infected persons:
 - Genotype (GT) 1 treated with PEG-INF + RBV + TVP/ BCP for 48 weeks:
 - TVP= SVR-12: 74%; BCP= SVR-12: 63%^{1,2}
 - Problem is NOT interferon-free regimen and the DDAs have interactions with antiretrovirals (ART)

1. Sulkowski et al., 2013a; 2. Sulkowski et al., 2013b

Treatment of HCV in HIV and HCV Co-Infected Patients

- Newer evidence shows the oral regimen of Simeprevir + Sofosbuvir effective for GT 1 HCV in HIV and HCV co-infected persons
 - Problem is simeprevir also interacts with same ART as Boceprevir and Telaprevir

Drug-Drug Interactions With DDAS and ART

Antiretroviral	Interactions With Boceprevir	Interactions With Telaprevir
Rilpivirine	No clinically relevant interactions	No clinically relevant interactions
Elvitegravir	No data	No clinically relevant interactions
Dolutegravir	No clinically relevant interactions	No clinically relevant interactions
Atazanavir/ritonavir	Coadministration not recommended	Coadministration not recommended
Darunavir/ritonavir	Coadministration not recommended	Coadministration not recommended
Efavirenz	Coadministration not recommended	Increase Telaprevir dose to 1125 mg q8h
Raltegravir	No clinically relevant interactions	No clinically relevant interactions

Rilpivirine [package insert]; Dolutegravir [package insert];
Custodio et al., 2013; DHHS 2013, Rhee et al., 2013

PHOTON-1 Study: Sofosbuvir + RBV for HCV in HIV Co-Infected Adults

- Study: Sofosbuvir 400 mg oral daily + RBV weight -N=115 Naïve HCV GT 1 for 24 weeks; SVR-12= 76%
 - N=26 Naïve HCV GT 2 for 12 weeks; SVR-12= 88%
 - N=42 Naïve HCV GT 3 for 12 weeks; SVR-12=67%
 - N=24 Treatment-experienced GT 2 for 24 weeks; SVR-12=92%
 - N=42 Treatment-experienced GT 3 for 24 weeks ; SVR-12= 94%

Future HCV Treatment for HIV Co-Infected Adults

- Other NS5B nucleotide and nonnucleotide and protease (NS3-4A) and NS5A inhibitors preliminarily show 95-98% SVR-12 in combination with each other and without ribavirin.
- Expected in the next 1 ½ years that there will be an all oral non-ribavirin based regimen to eradicate HCV in more than 95% of all patients mono-infected with HCV or co-infected with HCV & HIV.

HCV Treatment and OST Drug-Drug Interactions

- **Methadone** is metabolized by CYP450 3A4 hepatic enzymes and has high protein binding.
 - Telaprevir (TVP) ↓ AUC by 29% (but active free methadone remains unchanged): dose adjustment of methadone is not recommended
 - Boceprevir (BCP) ↓ methadone AUC by 22%, data from clinical studies does not suggest major interactions.
- **Buprenorphine** (BPN) is metabolized by CYP 450 3A4 and 3A5 and an inhibitor of CYP 450 3A4.
 - TVP ↓ the AUC of BPN by only 4%, without an effect of BPN on TVP
 - BPN AUC ↑ 19% during BCP treatment without clinical significance

HCV Treatment and OST Drug-Drug Interactions

- **Heroin** is a 3, 6-diacetyl derivative of morphine, metabolized by CYP450 3A4 ; an increase in drug levels is possible. No pharmacokinetic data are available.
- **Naltrexone**, no data are available.
- *Sofosbuvir does not yet have data reported with OST.

Hepatitis B (HBV)

Epidemiology of HBV Infection in Substance Using Individuals

- An estimated 800,000-1.4 million persons are infected with HBV in the U.S.^{1,2}
- An estimated 2,000-6000 deaths/year in the U.S. are due to HBV end-stage liver disease (ESLD)³
- HBV is a vaccine-preventable disease
- In 2006, U.S. adults aged > 20 years had the highest incidence of acute HBV infection
 - reflecting low HBV vaccination uptake among adults with behavioral risk for HBV (e.g. MSM, IDUS, persons with multiple sex partners).

Epidemiology of HBV Infection in Substance Using Individuals

- Sexual transmission is the major route of HBV transmission in the United States (38% of cases in U.S. and 25% are estimated to occur among MSM).
- Percutaneous transmission of HBV through injection drug use prevalence rates are estimated to be 5-10% globally.
- Hepatitis B surface antigen (HBs Ag) prevalence is 7.1% among PWID with HIV (associated with number of years of drug use and frequency of injection and sharing of drug preparation equipment)

Groups at High Risk for HBV Infection and Who Should be Screened:

- Individuals born in areas of high or intermediate prevalence rates for HBV including immigrants and adopted children
- U.S. born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity ($\geq 8\%$)
- Household and sexual contacts of HBsAg+ patients
- Persons who ever injected drugs
- Persons with multiple sexual partners or history of sexually transmitted diseases
- Men who have sex with men
- Inmates of correctional facilities
- Individuals with chronically elevated ALT or AST
- Individuals infected with HCV or HIV
- Patients undergoing renal dialysis
- All pregnant women
- Persons needing immunosuppressive therapy

Hepatitis B: Important Properties

- 42-nm enveloped virion (Dane particle)
- Nucleocapsid core containing partially double-stranded circular DNA genome
- Envelope contains a protein: surface antigen (HBsAg)
 - important for lab diagnosis
 - with resolved infection or vaccination one develops an antibody , HBs Ab)
- The core has DNA-dependent DNA polymerase
- Core antigen (HBcAg) that one can develop a Core Antibody to (HBc Ab)
- e-antigen (HBeAg)
 - HBeAg+ = higher transmissibility

HBV Serology and their Indications

- Resolution of infection is characterized by loss of HBs Ag and detection of the Antibody to HBs (HBs Ab), which confers protection against HBV infection and persists for life
- Persistence of HBsAg > 6 months indicates chronic infection
- Occasionally HBs Ag and HBs Ab coexist and they should be considered chronically infected
- **HB c Ab** can be detectable in acute and chronic infection and persists after recovery too
- **HBeAg** correlated with infectivity and conversion to **Hbe Ab** is an important therapeutic endpoint of Anti-HBV therapy

Natural History of HBV Infection

- 50% of patients who acquire acute HBV infection will transition to the inactive carrier state
- 30% progress to cirrhosis and the remainder to chronic hepatitis
- 20% of persons with chronic hepatitis from HBV will develop cirrhosis and ESLD and/ or hepatocellular carcinoma (HCC)
- Chronic Hepatitis has 4 phases: immune-tolerant, immune clearance, inactive and reactivation (see next slide)

Characteristics of Chronic HBV Hepatitis

Hepatitis B e Ag+ Immune Tolerant Chronic Hepatitis

HBeAg+, Normal ALT, High HBV DNA levels ($>10^7$)

Associated with perinatal acquisition

Mild disease on biopsy

Spontaneous clearance of HBe Ag is uncommon

Disease progression risk low, NO treatment

Inactive HB Surface Ag Carrier State

Antibody to HBe, normal ALT, Low or undetectable HBV DNA (<2000 IU/mL)

Liver biopsy shows minimal inflammation

Low rate of HBsAg clearance

Spontaneous HBeAg loss may be followed by HbeAg positivity in some

Requires lifelong Follow-up

Hbe Ag+ Active Chronic Hepatitis B

Hbe Ag+, elevated ALT, high HBV DNA level
biopsy mild disease to cirrhosis

10-20% spontaneously lose HbeAg

Hepatitis B e Antigen- Negative Active Chronic Hepatitis B

+ Anti Hbe, elevated ALT, and HBV DNA in serum

Consider patients for treatment

Serologic Tests and Their Interpretation

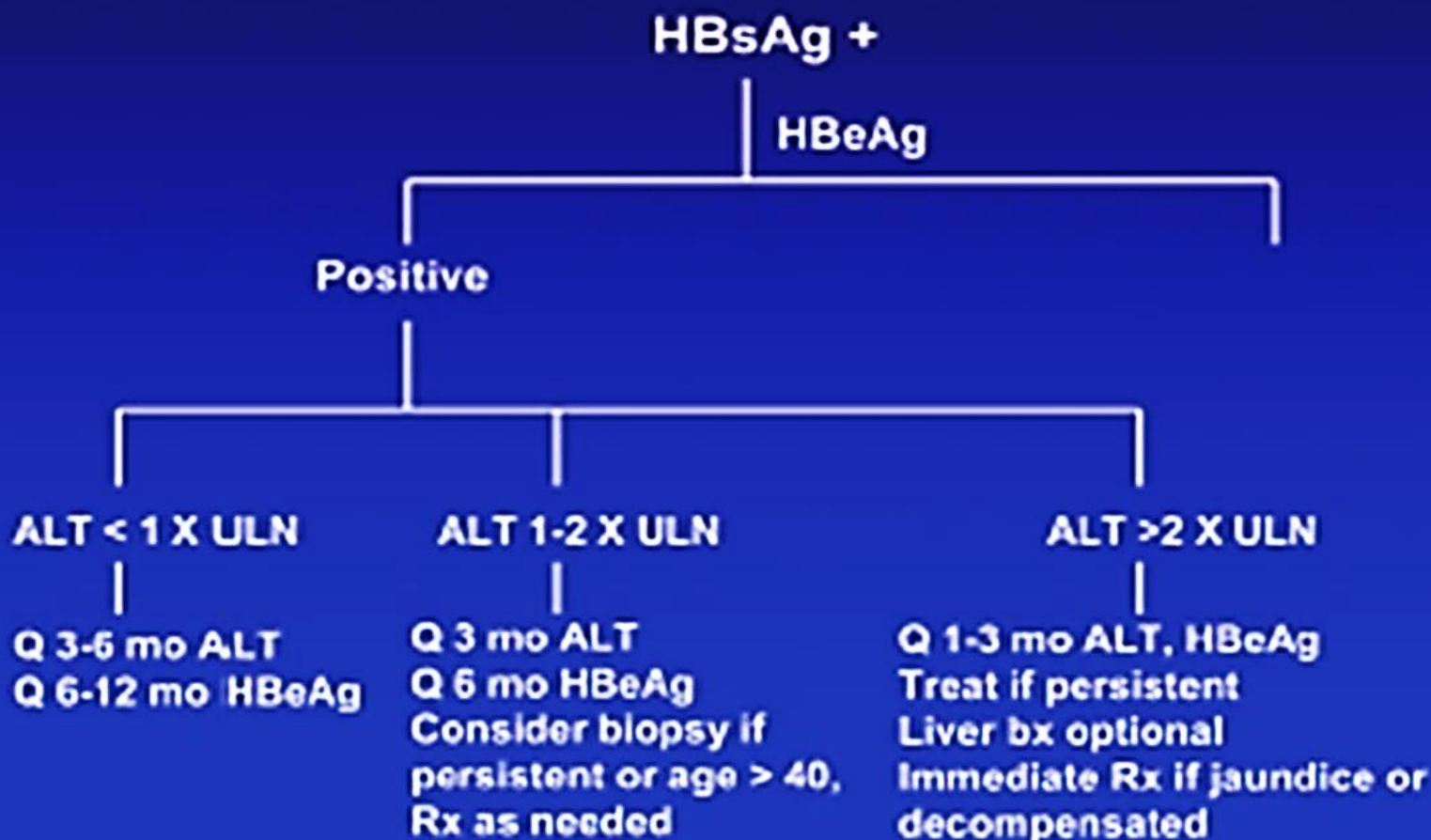
HBsAG	HBeAg	HBc IgM Ab	HBc IgG Ab	Hbe Ab	HBs Ab	Interpretation
+	+	+	-	-	-	Acute Hepatitis B
+	+	-	+	-	-	HBeAg+ Chronic HBC
+	-	-	+	+	-	HBeAg- Chronic HBC
-	-	-	+	+	+	Recovered
-	-	-	+	-	+	Chronic Hepatitis B or Passive transfer to infant born to HBs Ag+ mother or false positive
-	-	-	-	-	+	Vaccinated

Identification and Prevention to HBV Chronic Infection

- HBV chronic infection is evaluated for with a serologic test for Hepatitis B surface antigen (HBsAg) and Hepatitis B Surface antibody (HBsAb) recommended by the American Association of Liver Diseases (AASLD)^{1,2}
 - If HBsAg is negative and HBsAb is negative, then they should receive the Hepatitis B vaccination
 - If the HBsAg is negative and HBsAb is positive then this means they either were vaccinated or previously infected and cleared the infection.
 - If the HBsAg is positive and the HBsAb is negative then they require evaluation for active infection.
- If they are found to have active chronic infection, then the next steps are to determine if a liver biopsy is required or a non-invasive evaluation of liver fibrosis, or if treatment should be undertaken without biopsy.

A

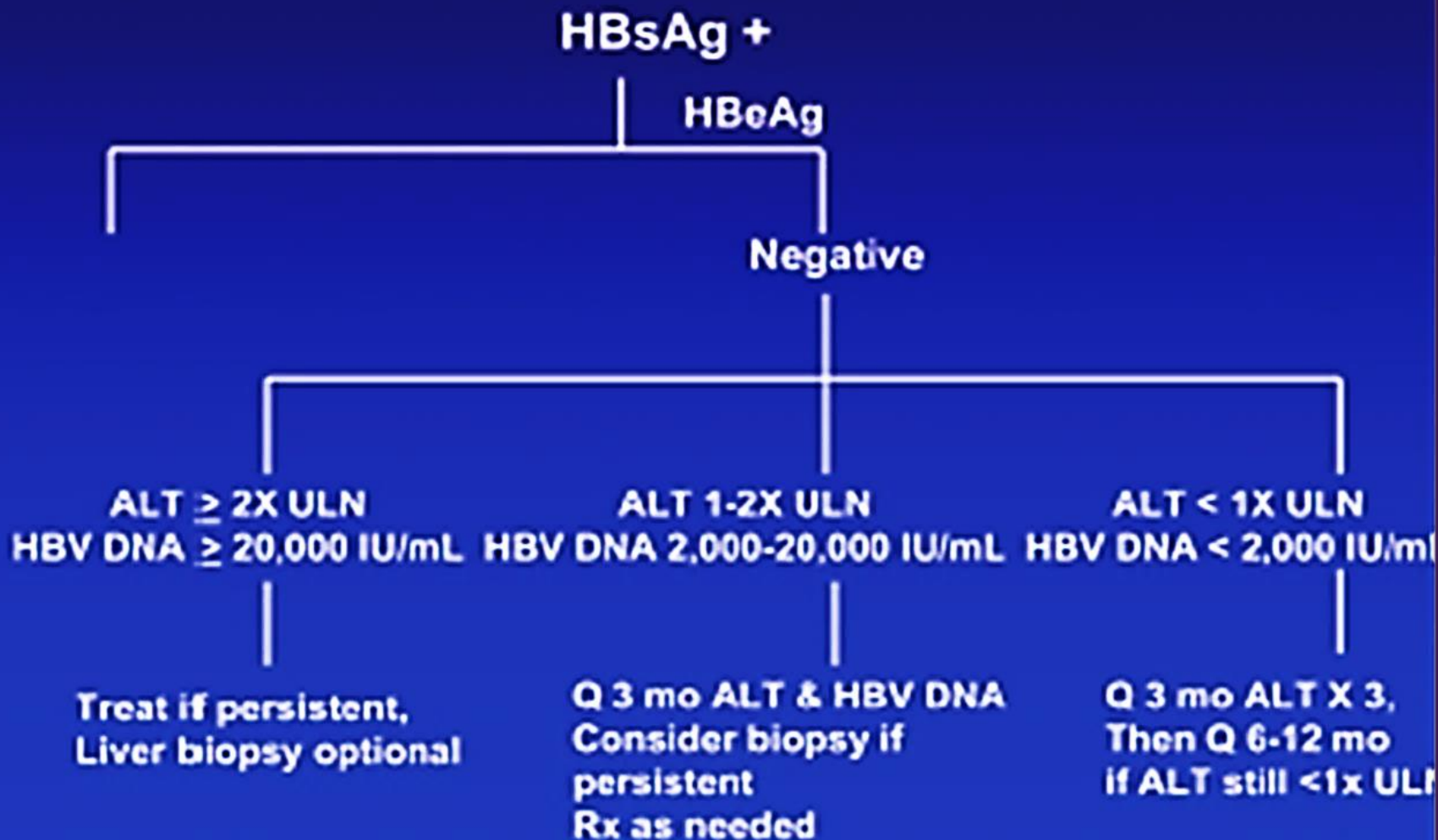
Management of Chronic HBV Infection*



* HCC surveillance if indicated

B

Management of Chronic HBV Infection*



* HCC surveillance if indicated

Chronic Hepatitis B Treatment Options

- FDA Approved for treatment of HBV chronic infection:
 - Interferon –alpha
 - Lamivudine
 - Adefovir
 - Entecavir
 - Telbivudine
 - Peg INF- alpha
 - Peg INF- alpha + Lamivudine
 - Tenofovir
- Available but not FDA-approved for treatment of HBV:
 - Emtricitabine
 - Truvada (Tenofovir + Emtricitabine)

Table 8. Responses to Approved Antiviral Therapies Among Treatment-Naïve Patients with HBeAg-Positive Chronic Hepatitis B

	Placebo/ Control Groups from Multiple Studies	Standard IFN- α 5 MU qd or 10 MU tiw 12-24 wk	Lamivudine 100 mg qd 48-52 wk	Adefovir 10 mg qd 48 wk	Entecavir 0.5 mg qd 48 wk	Tenofovir 300 mg qd 48 wk	Telbivudine 600 mg qd 52 wk	PegIFN α 180 mcg qw 48 wk	Peg IFN α 180 mcg qw + Lamivudine 100 mg 48 wk
Loss of serum HBV DNA*	0%-17%	37%	40%-44%	21%	67%	76%	60%	25%	69%
Loss of HBeAg	6%-12%	33%	17%-32%	24%	22%	na	26%	30%/34%†	27%/28%†
HBeAg seroconversion	4%-6%	Difference of 18%	16%-21%	12%	21%	21%	22%	27%/32%†	24%/27%†
Loss of HBsAg	0%-1%	7.80%	1%	0	2%	3.2%	0%	3%	3%
Normalization of ALT	7%-24%	Difference of 23%	41%-75%	48%	68%	68%	77%	39%	46%
Histologic Improvement	na	na	49%-56%	53%	72%	74%	65%	38%‡	41%‡
Durability of response		80%-90%	50%-80%§	~90%§	69%§	na	~80%	na	na

*Hybridization or branched chain DNA assays (lower limit of detection 20,000-200,000 IU/mL or 5-6 log copies/mL) in standard IFN- α studies and some lamivudine studies, and PCR assays (lower limit of detection approximately 50 IU/mL or 250 copies/mL) in other studies. na = not available.

†Responses at week 48 / week 72 (24 weeks after stopping treatment).

‡Post-treatment biopsies obtained at week 72.

§Lamivudine and entecavir - no or short duration of consolidation treatment, Adefovir and telbivudine - most patients had consolidation treatment.

Table 9. Responses to Approved Antiviral Therapies Among Treatment-Naïve Patients with HBeAg-Negative Chronic Hepatitis B

	Control/Placebo Groups from Multiple Studies	Standard IFN- α 5 Mu qd or 10 MU tiw 6-12 mo	Lamivudine 100 mg qd 48-52 wk	Adefovir 10 mg qd 48 wk	Entecavir 0.5 mg qd 48 wk	Telbivudine 600 mg qd 52 wk	Tenofovir 300 mg qd 48 wk	Peg IFNα 180 mcg qw 48 wk	PegIFN-α 180 mcg qw+ Lamivudine 100 mg qd 48 wk
Loss of serum HBV DNA*	0%-20%	60%-70%	60%-73%	51%	90%	88%	93%	63%	87%
Normalization of ALT	10%-29%	60%-70%	60%-79%	72%	78%	74%	76%	38%	49%
Histologic Improvement	33%	na	60%-66%	64%	70%	67%	72%	48%	38%†
Durability of response	Control	10%-20%	<10%	~5%	3%	na	na	~20%	~20%

na = not available

*Hybridization or branched chain DNA assays (lower limit of detection 20,000-200,000 IU/mL or 5-6 log copies/mL) in standard IFN-α studies and some lamivudine studies, and PCR assays (lower limit of detection approximately 50 IU/mL or 250 copies/mL) in other studies.

†Post-treatment biopsies obtained at week 72.

Special Issues with Treatment of HBV and HIV Co-Infected Individuals

- 5-10% of HIV-infected patients also have chronic HBV infection
- Progression to cirrhosis and ESLD and or HCC is more rapid in co-infected persons than those with HBV alone
- Emtricitabine (FTC), Lamivudine (3TC) and Tenofovir (TDF) are FDA-approved ART and effective against HIV and HBV
 - discontinuation of these drugs can cause serious hepatocellular damage resulting from reactivation of the HBV in co-infected persons

Special Issues with Treatment of HBV and HIV Co-Infected Individuals

- Entecavir has activity against HIV and HBV, but not FDA-approved for HIV alone as it is with HBV
 - its use for HBV treatment without ART in patients with dual infection will lead to an M184V mutation (confers resistance to 3TC and FTC), thus entecavir can only be used with other fully suppressive ART regimen in HIV/HBV co-infected persons
- 3TC resistance occurs in $\approx 40\%$ of patients after 2 years on 3TC alone, & $>90\%$ of patients after 4 years of 3TC alone
 - 3TC & FTC should be used in combination with other anti-HBV drugs in HIV+ pts

Treatment Recommendation of HIV in Patients Co-Infected with HIV and HBV

- All patients with +HBsAg should have an HBV DNA checked and evaluation for treatment based on current HBV guidelines^{1,2}
- The preferred regimen of ART for HIV and HBV co-infected adults who require HBV treatment and HIV treatment would include:
- Truvada (Tenofovir + Emtricitabine) or Tenofovir + lamivudine as the NRTI backbone with a fully suppressive ARV regimen²

Hepatitis A (HAV)

Hepatitis A (1)

- Hepatitis A is transmitted via the fecal-oral route, either through person-to-person contact or through consumption of contaminated food or water.
- Although Hepatitis A infection does not develop into chronic infection as HBV and HCV infection may, it can cause serious exacerbations in liver disease for those with concurrent HCV and HBV infection
- Vaccination is the most effective way to prevent HAV transmission among persons at risk for infection (illegal drug users, MSM, and persons with chronic liver disease)

Hepatitis A (2)

- Screening via serologic testing is required to diagnosis active HAV infection or history of exposure/ vaccination
- A positive IgM Hepatitis A antibody indicates acute HAV infection
- A positive IgG or Total Hepatitis A antibody indicates previous infection or possible prior vaccination; however if IgM is positive then a positive total or IgG HAV antibody would indicate current infection

Pre-vaccination Serologic Testing for Hepatitis A Vaccination Susceptibility

- Almost 1/3 of the U.S. population have serologic evidence of previous HAV infection (increases with age)
- Screening for HAV may be cost-effective in populations where prevalence of HAV infection is high (e.g. persons ages >40 years and person born in high HAV endemicity)
- Hepatitis A IgG antibody should be offered, and if negative then persons should be offered the vaccine

Pre-vaccination Serologic Testing for Susceptibility to HAV

- Pre-exposure Vaccination after assessment with Hepatitis A IgG antibody is found to be negative is recommended for:
 - All MSM
 - Illegal drug users of both injection and non-injection drugs
 - Persons with chronic liver disease, including persons with chronic HBV and HCV infection
 - Persons with HIV infection

Summary: Recommended Serologic testing of Hepatitis A, B & C for Substance Using Individuals

- **Hepatitis C Infection:**
 - Check HCV Antibody
 - if HCV Ab is Positive check HCV RNA level
 - if RNA level positive, refer to expert for evaluation
 - If RNA negative, then no need to retest, Antibody confers lifelong immunity
 - If HCV Antibody negative:
 - Counseling about prevention and retest every 6 months if engaging in risk behaviors (previously discussed in presentation)
- **Hepatitis B Infection:**
 - Check Hepatitis B Surface Antibody & Hepatitis B Surface Antigen
 - If HBV surface Antigen is negative, and HBV surface antibody is positive-nothing more to do, no need to retest , confers lifelong immunity
 - If HBV surface Antigen is positive, check HBV DNA , obtain Liver Function Tests and refer to expert for evaluation
 - If HBV surface Antigen is negative and Surface Antibody is negative, then vaccinate; no need to retest after finishing vaccination series
- **Hepatitis A Infection:**
 - Check Hepatitis A IgG antibody routine screen:
 - If Hepatitis A IgG antibody is negative, vaccinate
 - If Hepatitis A IgG is positive, no need to retest; confers lifelong immunity.

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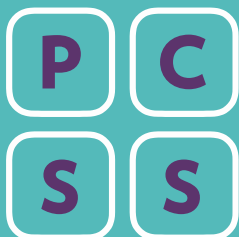
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