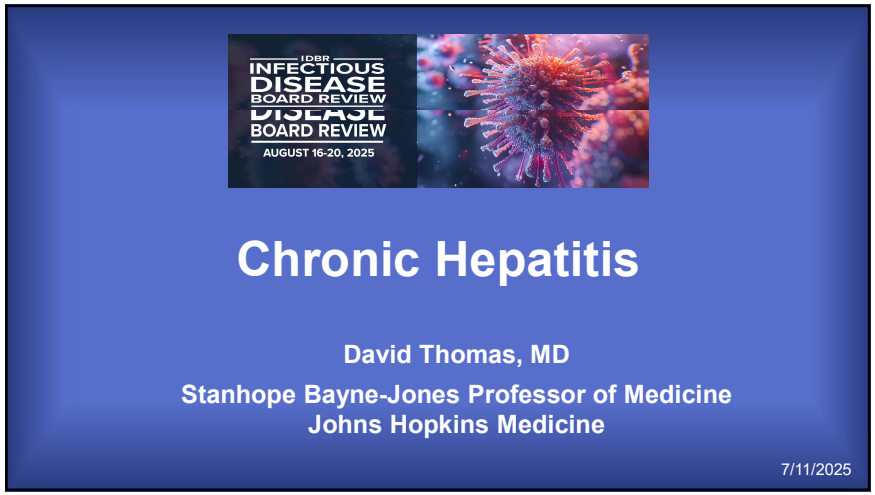
19 Chronic Hepatitis

Speaker: David Thomas, MD



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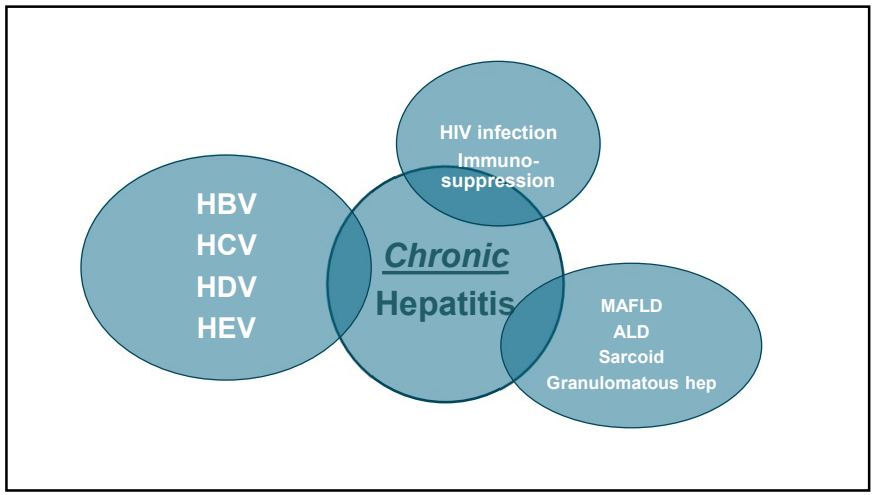

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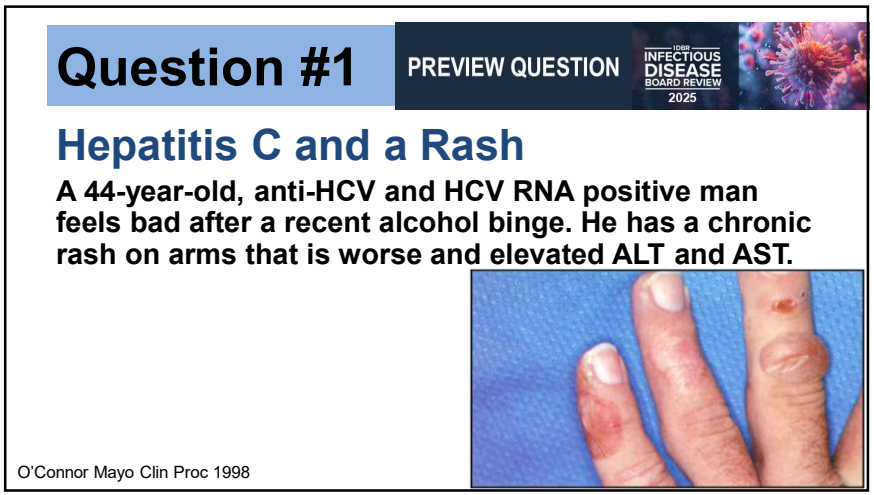

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Question #1

PREVIEW QUESTION

IDBR INFECTIOUS DISEASE BOARD REVIEW 2025

HCV with a Rash

What is the most likely dx?

A. Cirrhosis due to HCV and alcohol
B. Necrolytic acral erythema
C. Porphyria cutanea tarda
D. Essential mixed cryoglobulinemia
E. Yersinia infection

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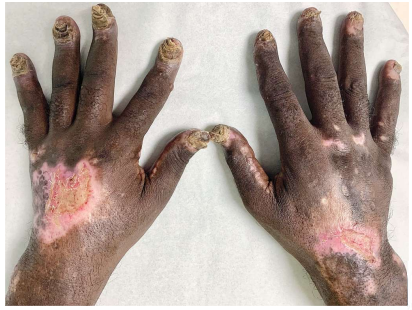
6

Porphyria Cutanea Tarda Associated with Hepatitis C

Tejesh S. Patel, M.D., and Evgeniya Teterina Mohammed, M.D.



June 10, 2021
N Engl J Med 2021; 384:e86

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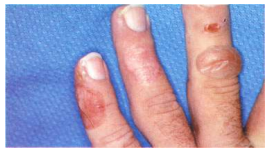
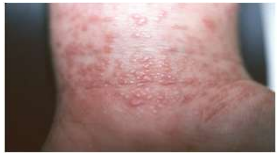
Compare

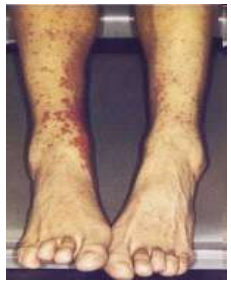
Porphyria cutanea tarda



Lichen planus



Cryoglobulin vasculitis

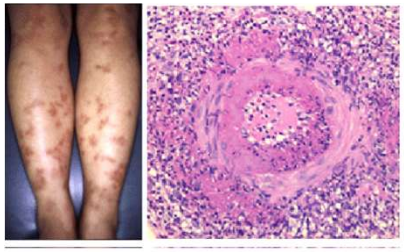


blogspot.com; O'Connor Mayo Clin Proc 1998

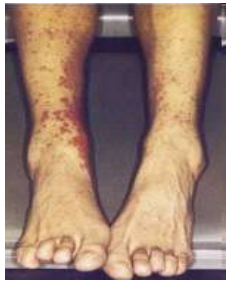
8

Compare

HBV: Polyarteritis nodosa



HCV: Cryoglobulin vasculitis



blogspot.com; OConnor Mayo Clin Proc 1998; Chen Rheum 2014

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Question #2

What is true regarding testing for HCV antibodies?

A. Testing indicated only for those with risk
B. New 4th generation antibody/ag test sensitive for acute infection
C. Indicated for pregnant women
D. Repeat after cure if new exposures
E. Often falsely negative in persons with HIV

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Question #2

What is true regarding testing for HCV antibodies?

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C. **Indicated for pregnant women ***
D. Repeat after cure if new exposures
E. Often falsely negative in persons with HIV

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IDSA/AASLD Guidelines

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy.	I, B
Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP).	IIa, C

RECOMMENDATION The USPSTF recommends screening for HCV infection in adults aged 18 to 79 years. (B recommendation)

JAMA. doi:10.1001/jama.2020.1123
Published online March 2, 2020.

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Question #3

- 54-year-old man was anti-HCV pos after routine screen by primary. RNA also pos; moderate ETOH; otherwise well.
- CMP and CBC were normal.

Which of these is most necessary before treatment?

A. HCV genotype
B. HCV 1a resistance test
C. Elastography
D. HBsAg
E. Repeat in 6 months to be sure chronic

13

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D. **HBsAg ***
E. Repeat in 6 months to be sure chronic

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U.S. Food and Drug Administration Protecting and Promoting Your Health | Drug Safety Communications

FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C

All are tested for HBV

- HBsAg pos: treat per HBV guidelines
- Anti-HBc pos: monitor

Bersoff-Macha Ann Intern Med 2017; Thio and Balagopal CID 2015

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Staging is Needed to Assess for Cirrhosis (But Not Most Urgent)

Accepted staging methods	Not for routine staging
1. Liver biopsy	1. Viral load
2. Blood markers	2. HCV genotype
3. Elastography	3. Ultrasound
4. Combinations of 1-3	4. CT scan or MRI

Hcvguidelines.org

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HCV NS5 RAS Testing is Uncommonly Recommended

Regimen-Specific Recommendations for Use of RAS Testing in Clinical Practice

RECOMMENDED	RATING
Elbasvir/grazoprevir NS5A RAS testing is recommended for genotype 1a-infected, treatment-naive or -experienced patients being considered for elbasvir/grazoprevir. If present, a different regimen should be considered.	I, A
Ledipasvir/sofosbuvir NS5A RAS testing can be considered for genotype 1a-infected, treatment-experienced patients with and without cirrhosis being considered for ledipasvir/sofosbuvir. If clinically important[a] resistance is present, a different recommended therapy should be used.	I, A
Sofosbuvir/velpatasvir NS5A RAS testing is recommended for genotype 3-infected, treatment-naive patients with cirrhosis and treatment-experienced patients (without cirrhosis) being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added or another recommended regimen should be used.	I, A

[a] Clinically important = ≥100-fold shift in the in vitro EC_{50} to ledipasvir

NB: no PI resistance testing
Clinically sig is >100-fold in vitro

Wyles, HCVguidelines.org

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Question #4

54-year-old with HCV

Elastography (17.3 kPa) and Fib-4 (5.5) consistent with cirrhosis. Genotype 1a; HBsAg neg; Ultrasound and UGI are okay. You recommend treatment but he wants to know why.

Which is NOT true of successful treatment?

A. Reduces risk of reinfection
B. Reduces risk of death
C. Reduces risk of HCC
D. Reduces risk of liver failure

18

Question #4

54-year-old with HCV

Elastography (17.3 kPa) and Fib-4 (5.5) consistent with cirrhosis. Genotype 1a; HBsAg neg; Ultrasound and UGI are okay. You recommend treatment but he wants to know why.

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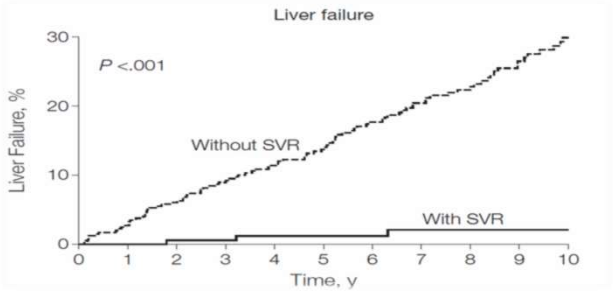
19

SVR Reduces Clinical Outcomes



Van der Meer, *JAMA* 2012. Backus, *Clin Gastro* 2011. Imazeki, *Hepatology* 2003. Shiratori, *Ann Intern Med* 2005. Veldt, *Ann Intern Med* 2007. Berenguer, *Hepatology* 2009.

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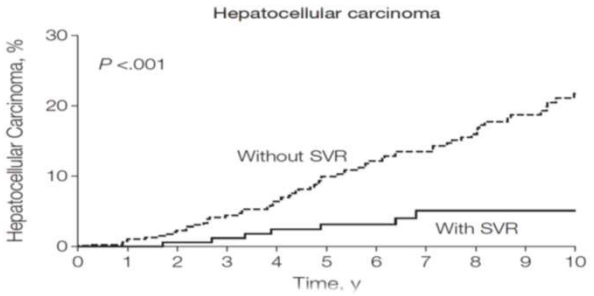
SVR Reduces Clinical Outcomes



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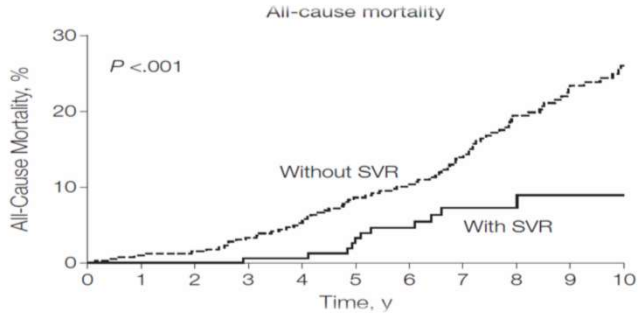
SVR Reduces Clinical Outcomes



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Question #5

54-year-old with HCV

Which is true of initial HCV treatment?

A. Avoid sofosbuvir if renal insufficiency
B. Avoid glecaprevir (PI) if on atorvastatin
C. Avoid sofosbuvir/ledipasvir if genotype 1
D. Prolong treatment if person also has HIV

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Question #5

54-year-old with HCV

Which is true of initial HCV treatment?

A. Avoid sofosbuvir if renal insufficiency
B. Avoid glecaprevir (PI) if on atorvastatin *
C. Avoid sofosbuvir/ledipasvir if genotype 1
D. Prolong treatment if person also has HIV

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AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA Infectious Diseases Society of America

Test, Evaluate, Monitor | Treatment-Naive | Treatment-Experienced | Unique & Key Populations

Recommended regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.
For patients with HIV/HCV coinfection, a treatment duration of 12 weeks is recommended.

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HCV-HIV ART Drug Interactions

		Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Protease Inhibitors	Boosted Atazanavir	A	A			
	Boosted Darunavir	A	A			
	Boosted Lopinavir	ND, A	A			ND
NNRTIs	Doravirine		ND		ND	ND
	Efavirenz				ND	ND
	Rilpivirine					
	Etravirine	ND	ND	ND	ND	ND
Integrase Inhibitors	Bictegravir			ND	ND	
	Cabotegravir	ND	ND	ND	ND	ND
	Cobicistat-boosted elvitegravir	C	C			C
	Dolutegravir					ND
	Raltegravir					ND
Entry Inhibitors	Fostemsavir	ND	ND	ND	ND	ND
	Ibalizumab-uiyk	ND	ND	ND	ND	ND
	Maraviroc	ND	ND	ND	ND	ND
NRTIs	Abacavir		ND	ND		ND
	Emtricitabine					
	Lamivudine		ND	ND		ND
	Tenofovir disoproxil fumarate	B, C	B, C			C
	Tenofovir alafenamide	D	D	ND		D

www.hcvguidelines.com

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HCV Treatment Summary

- Test and treat (and stage)
- Two pangenotypic regimens: SOF/VEL and G/P
- Watch for HBV relapse at week 8 if HBsAg pos
- No change for HIV (avoid drug interactions), renal insufficiency, acute infection
- Compensated cirrhosis same for G/P and SOF-based except GT3 with resistance

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Hepatitis B: 2023 Testing Recs for USA

Universal hepatitis B virus (HBV) screening
- HBV screening at least once during a lifetime for adults aged ≥18 years (new recommendation)
- During screening, test for hepatitis B surface antigen (HBsAg), antibody to HBsAg, and total antibody to HBcAg (total anti-HBc) (new recommendation)

Screening pregnant persons
- HBV screening for all pregnant persons during each pregnancy, preferably in the first trimester, regardless of vaccination status or history of testing*
- Pregnant persons with a history of appropriately timed triple panel screening and without subsequent risk for exposure to HBV (i.e., no new HBV exposures since triple panel screening) only need HBsAg screening

Risk-based testing
- Testing for all persons with a history of increased risk for HBV infection, regardless of age, if they might have been susceptible during the period of increased risk†
- Periodic testing for susceptible persons, regardless of age, with ongoing risk for exposures, while risk for exposures persists†

MMWR March 10, 2023

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Question #6

After HBV testing, which person requires treatment?

1. 41 yr male in China HBsAg pos, HBeAg neg, anti-HBe pos, ALT 78 IU/ml, AST 86 IU/ml, HBV DNA 5,600
2. 51 yr male HBsAg neg, anti-HBc pos, HBeAg neg, anti-HBe pos, ALT 48 IU/ml, AST 36 IU/ml, HBV DNA neg
3. 18 yr woman born in Viet Nam HBsAg pos, HBeAg pos, anti-HBe neg, ALT 18 IU/ml, AST 16 IU/ml, HBV DNA 8.2 mil
4. 62 yr woman about to start hydroxychloroquine for SLE anti-HBc pos, HBsAg neg, HBeAg neg, anti-HBe pos, DNA neg, ALT 34 IU/ml, AST 28 IU/ml
5. 19 yr man about to start college anti-HBs pos, HBsAg neg, HBeAg neg, DNA neg, ALT 18 IU/ml, AST 12 IU/ml

29

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After HBV testing, which person requires treatment?

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After HBV Testing, Which Requires Treatment

Age (yrs)	DNA (IU/ml)	ALT (IU/ml)	Issue/interpretation
41	**5600**	**78**	**Chronic HBV with replication and inflammation**
51	Neg	48	Isolated core/possible occult HB. Probable MASLD
21	8,200,000	18	High replication without inflammation (immunotolerant)
62	Neg	34	Isolated core/possible occult. Mild immunosuppression
19	Neg	18	Vaccinated

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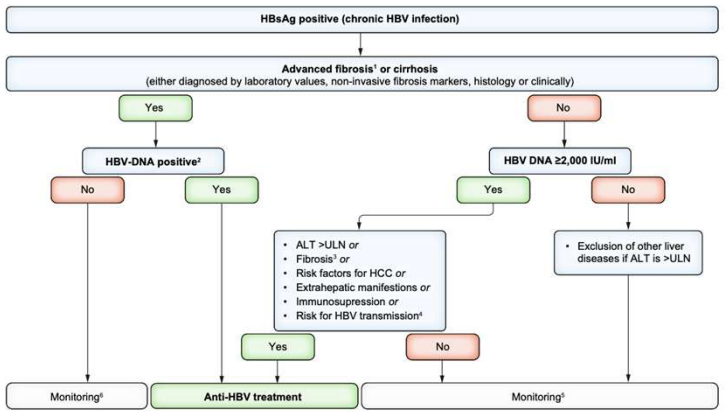

EASL J Hepatol 2025

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Treatment of Chronic Hepatitis B (HBsAg pos)

- **Disease (ALT and/or biopsy and/or elastography) + Replication (HBV DNA > 2,000 IU/ml)**
- **Cirrhosis- treat all**
- **HIV – treat all**
- **Pregnancy- treat if HBV DNA > 200,000 IU/ml**
- **New threshold to treat is dropping (EASL May 2025; AASLD summer 2025)**

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Evaluation of Persons with CHB

- **HIV, HBV DNA, anti-HDV, HBeAg**
- **Genotype if IFN considered; q HBsAg if 'covered'**
- **Stage (liver enzymes and/or elastography or biopsy)**
- **Renal status**
- **US to r/o HCC**
  - **Cirrhosis: all**
  - **Asian: male 40; female 50**
  - **African: 25-30**

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Four Preferred Treatments for Chronic Hepatitis B

HBeAg Positive	Peg-IFN*	Entecavir†	Tenofovir Disoproxil Fumarate†	Tenofovir Alafenamide‡
% HBV-DNA suppression (cutoff to define HBV-DNA suppression)§	30-42 (<2,000-40,000 IU/mL) 8-14 (<80 IU/mL)	61 (<50-60 IU/mL)	76 (<60 IU/mL)	73 (<29 IU/mL)
% HBeAg loss	32-36	22-25	—	22
% HBeAg seroconversion	29-36	21-22	21	18
% Normalization ALT	34-52	68-81	68	—
% HBsAg loss	2-7 11 (at 3 years posttreatment)	4-5	8	1
HBeAg Negative	**Peg-IFN**	**Entecavir**	**Tenofovir Disoproxil Fumarate†**	**Tenofovir Alafenamide‡**
% HBV-DNA suppression (cutoff to define HBV-DNA suppression)‖	43 (<4,000 IU/mL) 19 (<80 IU/mL)	90-91 (<50-60 IU/mL)	93 (<60 IU/mL)	90 (<29 IU/mL)
% Normalization ALT¶	59	78-88	76	81
% HBsAg loss	4 6 (at 3 years posttreatment)	0-1	0	<1

TAF 25 mg with or without FTC

AASLD guidelines, Terrault Hepatology 2018

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Treatment of HBV Changes with Renal Insufficiency

- **GFR 30-60 mL/min/1.73 m^2** : TAF 25 mg preferred
- **GFR <30-10:** TAF 25mg OR entecavir 0.5 mg q 3d
- **GFR <10 no dialysis:** entecavir 0.5 mg
- **Dialysis:** TDF 300mg/wk PD or entecavir 0.5mg/wk or TAF 25mg PD

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HIV/HBV Coinfected Need Treatment for Both

- **All are treated and tested for both**
- **HBV-active ART**
- **Entecavir less effective if LAM exposure**
- **Watch switch from TAF- or TDF-containing regimen**

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It Is Hard to Stop HBV Treatment

- **If HBeAg conversion noted and no cirrhosis *consider* stopping after 6 months**
- **HBeAg neg when treatment started and all with cirrhosis stay on indefinitely**
  - **(Newer practice is to use quantitative HBsAg and stop only when low (eg <100))**

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Question #7

Hepatitis serology in the oncology suite

- You are called about 62-year-old Vietnamese scientist who is in oncology suite where he is about to get R-CHOP for Non-Hodgkins lymphoma.
- Baseline labs: normal AST, ALT, and TBili. Total HAV detectable; anti-HBc pos; HBsAg neg; anti-HCV neg.

What do you recommend?

A. Hold rituximab
B. Hold prednisone
C. Entecavir 0.5 mg
D. HCV PCR

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What do you recommend?

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C. Entecavir 0.5 mg *
D. HCV PCR

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Rituximab, High-dose Prednisone, and BM Transplant for HBV Reactivation

- **If HBsAg pos, prophylaxis *always* recommended**
- **If anti-HBc pos but HBsAg neg, prophylaxis still recommended with high-risk exposures (anti-CD20, high dose Pred, BM tx)**
- **Use TAF or ETV for 6-12 mo after dc immunosuppression (12 for anti-CD20)1**

AASLD Terrault Hepatology 2018

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Question #8

Chronic hepatitis in a transplant recipient

- **51 y/o HTN, and ankylosing spondylitis s/p renal transplant presents with elevated liver enzymes. Pred 20/d; MMF 1g bid; etanercept 25mg twice/wk; tacro 4mg bid. Hunts wild boar in Texas**
- **HBsAg neg, anti-HBs pos, anti-HBc neg; anti-HCV neg; HCV RNA neg; CMV IgG neg; EBV neg; VZV neg. ALT 132 IU/ml, AST 65 IU/ml; INR 1. ALT and AST remained elevated; HBV, HCV, HAV, CMV, EBV serologies remain neg.**

Barrague Medicine 2017

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Question #8

Which test is most likely abnormal?

1. HEV PCR
2. HCV IgM
3. Tacrolimus level
4. Adenovirus PCR
5. Delta RNA PCR

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Question #8

Which test is most likely abnormal?

1. **HEV PCR ***
2. HCV IgM
3. Tacrolimus level
4. Adenovirus PCR
5. Delta RNA PCR

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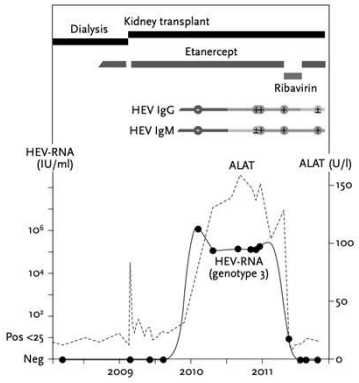
Chronic HEV in Transplant Recipient

- Europe (boar)
- Can cause cirrhosis
- Tacrolimus associated
- Ribavirin may be effective



Barrague Medicine 2017

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Chronic Hepatitis for the Boards Summary

- HCV-associated conditions: PCT or cryoglobulinemia
- HCV: HBV relapse or drug interaction
- HBV: relapse post rituximab
- HEV: chronic in transplant patient

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Thanks and good luck on the test!

Questions:

Dave Thomas
- dthomas@jhmi.edu

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