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Gastroenterology & Hepatology
Advanced Practice Providers

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HBV Virus Reactivation

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Disclosures

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Disclosures

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Speakers Bureau: Intercept, Clinical Area- NASH

AASLD Guidelines for Screening and Treatment of HBV in Patients Requiring Immunosuppression

- HBsAg and anti-HBc testing should be performed in patients who are to receive immunosuppressive, cytotoxic or immunomodulatory therapy
- HBsAg-positive, anti-HBc–positive patients should initiate anti-HBV prophylaxis before immunosuppressive or cytotoxic therapy.
- HBsAg-negative, anti-HBc–positive patients could be carefully monitored with ALT, HBV DNA, and HBsAg with the intent for on-demand therapy, except for patients receiving anti-CD20 antibody therapy (e.g., rituximab) or undergoing stem cell transplantation, for whom anti-HBV prophylaxis is recommended.
- LAM can be used if the anticipated duration of treatment is short (≤ 12 months) and baseline serum HBV DNA is not detectable
- TDF or ETV is preferred if longer duration of treatment is anticipated.

LAM=lamivudine, LdT=telbivudine.

Terrault, N. et al. “Practice Guidance”; *Hepatology.* 2018;50(3):1-36.

AGA Guideline on Prevention and Treatment of HBVr During Immunosuppressive Drug Therapy

AGA recommendation based on risk gradient with different immunosuppressive drugs based on estimates of reactivation

High-risk (>10%) Moderate-risk (1-10%) Low-risk (<1%)

	HBsAg+/ HBcAb+	HBsAg-/ HBcAb+
B cell-depleting agents (e.g., rituximab, ofatumumab)		
Anthracycline derivatives (e.g., doxorubicin, epirubicin)		
High-dose (> 20 mg prednisone daily or equivalent) corticosteroids daily for ≥ 4 weeks		
Moderate-dose (10-20 mg prednisone daily or equivalent) corticosteroids daily for ≥ 4 weeks		
TNF alpha inhibitors (e.g., etanercept, adalimumab, certolizumab, infliximab)		
Cytokine or integrin inhibitors (e.g., abatacept, ustekinumab, natalizumab, vedolizumab)		
Tyrosine kinase inhibitors (e.g., imatinib, nilotinib)		
Low-dose (< 10 mg prednisone daily or equivalent) corticosteroids for duration of ≥ 4 weeks		
Any dose of oral corticosteroids daily for ≤ 1 week		
Intra-articular corticosteroids		
Traditional immunosuppressive agents (e.g., azathioprine, 6-mercaptopurine, methotrexate)		

HBVr, hepatitis B virus reactivation; anti-HBc-positive; HBVr: HBV virus Reactivation.

Reddy KR, et al. *Gastroenterology.* 2015;148:215–219.

AGA Guideline on Prevention and Treatment of HBVr During Immunosuppressive Drug Therapy

AGA recommendation based on risk gradient with different immunosuppressive drugs based on estimates of reactivation

	High-Risk	Moderate-Risk	Low-Risk
Anticipated incidence of HBVr	> 10%	1-10%	< 1%
AGA Recommendation	Antiviral prophylaxis during IS & for at least 6-12 months after D/C of IS therapy	Antiviral prophylaxis during IS & for at least 6 months after D/C of IS therapy	No antiviral prophylaxis

High-risk group: HBsAg+/HBcAb+ or HBsAg-/HBcAb+ treated with B cell-depleting agents, or HBsAg+/HBcAb+ treated with anthracycline derivatives, moderate- or high-dose corticosteroids daily for ≥ 4 weeks.
Moderate-risk group: HBsAg+/HBcAb+ or HBsAg-/HBcAb+ treated with TNF alpha inhibitors, other cytokine or integrin inhibitors, tyrosine kinase inhibitors, HBsAg+/HBcAb+ treated with low-dose corticosteroids for duration of ≥ 4 weeks, HBsAg-/HBcAb+ treated with moderate- or high-dose corticosteroids daily for ≥ 4 weeks or anthracycline derivatives.
Low-risk group: HBsAg+/HBcAb+ or HBsAg-/HBcAb+ treated with traditional immunosuppressive agents, intra-articular corticosteroids, any dose of oral corticosteroids daily for ≤ 1 week, or HBsAg-/HBcAb+ treated with low-dose corticosteroids for ≥ 4 weeks.
Reddy KR, et al. *Gastroenterology.* 2015;148:215–219.

Case Study 1

HISTORY & PE | MEDICATIONS | LABS | PROGRESS NOTES | OTHER

- Mr. Wang, 79 y/o M, immigrated from Taiwan in the 60's.
- History of Chronic Hepatitis B seroconversion.
- Developed HCC in late 2019. HCC resected in early 2020 with clean margin.
- Lung metastasis discovered in July. Will undergo immunotherapy with atezolizumab and bevacizumab.
- Current HBV serology: HBV sAg (-), sAb (+).
- Need HBV reactivation prophylaxis before immunotherapy?

Reference: Zhang, X. et al. PD-1 PD-L1.

Case Study 2

HISTORY & PE | MEDICATIONS | LABS | PROGRESS NOTES | OTHER

- Ms. Patel, 46 y/o F, born and raised in New Jersey
- Never tested for HBV serology until a few months ago when found to have ovarian cancer and was preparing to undergo chemotherapy
- Current HBV serology HBV cAb (+), sAb (+), sAg (-)
- HBVr risk category? Need sAb titer
- Need HBV reactivation prophylaxis before chemo starts?

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Management of Chronic Hepatitis B in Pregnancy: A Case-based Approach

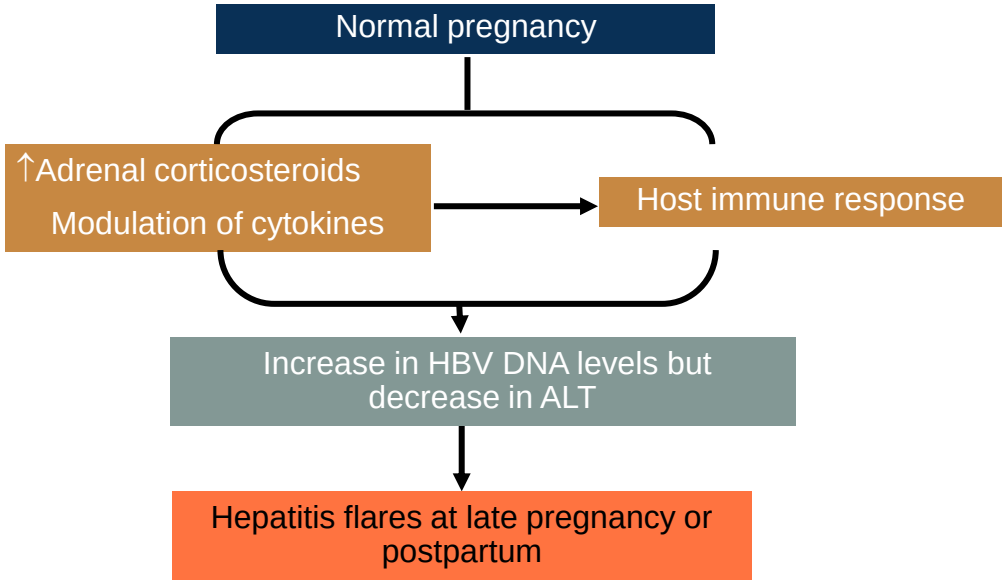
Case Study

- Patient Profile: 32 y/o female with established diagnosis of CHB. 11 weeks pregnant and referred by her OB/GYN for elevated liver enzymes. HBV infection controlled on TDF, which she stopped 3 weeks ago when she found out that she’s pregnant. She has concerns on the fetal exposure to anti-viral and prefers not to be treated.
- Presenting Symptoms: None
- Which tests/labs should be ordered?

Results of Tests/Labs

- Lab Results
  - HBsAg positive, HBeAg negative, HB eAb positive
  - HBV DNA 25,000 IU/ml
  - AST 20
  - ALT 50
  - Albumin 4.5
  - Platelets 225
  - T Bilirubin 0.7

Effects of Pregnancy on Chronic HBV Infection



Tan HH. et al. *Hepatol Int.* 2008: 370-5; Nguyen G et al. *Aliment Pharmacol Ther*. 2009: 755-64; ter Borg MJ. et al. *J Viral Hepatol*. 2008; 15: 37-41.

Questions

- Is this patient’s ALT a call for continuing treatment? If you decide not to treat, at what level of ALT and/or viral load you might reconsider treatment?
- What other work up needed for her elevated ALTs and how to monitor it during her pregnancy?

Decision Making

- You recommended starting TdF monotherapy, however she deferred the treatment but agreed to a follow up visit in 4 weeks.
- She instead returns at gestation week 20, uncomplicated pregnancy. Asymptomatic.
- PE: normal exam.
- Labs: AST 20, ALT 43.
- HBV DNA 280,000,000 IU/mL.
- NL Albumin, Platelet count, and T Bilirubin.

- What do you recommend now?
- Any additional information?

Recommendations From Association Guidelines for Preventing HBV MTCT

EASL	2017	TDF LAM, LdT	Second trimester of pregnancy	HBV DNA >2x10^5 IU/mL, HBsAg levels > 4 logs IU/mL
AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES	2018	TDF LAM, LdT	28-32 weeks of gestation	HBV DNA >2×10^5 IU/mL.
APASL	2015	TDF, LdT	28-32 weeks of gestation	HBV DNA >$10^{6–7}$ IU/mL

Treatment Options

- *Category B:* Telbivudine (HBV), Tenofovir-DF (HBV), Tenofovir-AF (HIV)
- *Category C:* Lamivudine (HBV), Adefovir, Entecavir
- **Pregnancy category B:**
  - Animal studies do not indicate a risk to the fetus and there are no controlled human studies, or animal studies show an adverse effect on the fetus but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus
- **Pregnancy category C:**
  - Studies have shown that the drug exerts animal teratogenic or embryocidal effects, but there are no controlled studies in women, or no studies are available in either animals or women

Not Classified for HBV in 2016 Tenofovir alafenamide (TAF)

- If you offer treatment, what are your treatment goals?
  - ALT
  - HBV-DNA
  - Reduction in MTCT
- What would you recommend for Rx?
- After the baby is born, would you consider continuing HBV therapy or would you consider stopping the medication?

- Post Partum what do you recommend?
  - Stop therapy
  - Change therapy
- How do you monitor her?

Patient Follow-Up

- Patient Care
  - Short-term plan
    - Timing including additional labs, procedures, clinic visits
  - Long-term plan
    - Does the patient stay with you? If so, for how long?
    - Do you release back to PCP/OB-GYN? If so, at what point?