

Issues in Liver Health and Disease: Overview for the Nonhepatologist

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe changing epidemiology of viral hepatitis
- Describe new hepatitis B vaccine strengths and limitations
- Know when and how to screen for NAFLD/NASH

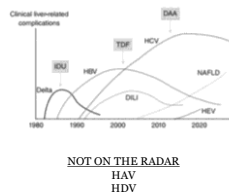
AUDIENCE RESPONSE QUESTION 1

- A 40 yo homeless man with HIV infection presents to ED with mental status changes.
- Physical Exam: Malnourished man, icteric sclera, abdominal tenderness on RUQ palpation, + asterixis
- Which is of the following is most likely?

AUDIENCE RESPONSE QUESTION 1... Which is of the following is most likely?

1. Acute hepatitis A
2. Acute hepatitis B
3. Decompensated chronic hepatitis B
4. Decompensated chronic hepatitis C
5. Hepatitis D superinfection
6. Acute hepatitis E

EVOLUTION OF LIVER INJURY IN HIV



Sherman KE et al, HEPATOLOGY COMM, 2017

TOPICS

- VIRAL HEPATITIS
 - Changing Epi and New Concerns
 - HBV New Vaccine
- NAFLD/NASH
 - Increased Recognition
 - New Therapies?

HEPATITIS A

- Increase frequency of reporting
 - <2000 Cases reported by CDC in 2016
 - >7000 Cases reported by CDC in October, 2018
- Significant increase seen in European cities among MSM

Arkansas Officials Warn Of Another Possible Hepatitis A Exposure.
The 21st (10/10/18) reports the Arkansas Department of Health is warning about another potential hepatitis A exposure in "an employee of Murdock's Cattle in Jonesboro" who tested positive.

Multistate outbreak of Hepatitis A linked to smoothies - CDC

CDC reports 119 people from 8 states have Hepatitis A linked to smoothies
BY NEWS DESK | SEPTEMBER 16, 2016 The U.S. Centers for Disease Control and Prevention (CDC) updated this outbreak on Friday afternoon to a total of 119 cases of Hepatitis A from eight states. Forty-seven of these individuals have been hospitalized, but no related deaths are being reported.

workers mean for you? Eight questions answered
Terry DeMio and Anne Saker,
Cincinnati Enquirer
Published 10:50
pm EDT Updated 10:50 am EDT Sept 17, 2016

FDA Investigates Outbreak of Hepatitis A Illnesses Linked to Raw Scallops in Hawaii- August 24, 2016

Confirmed case count hits 168 in Hawaii Hepatitis A outbreak
BY CATHY MCGRAW | AUGUST 10, 2016 The confirmed case count in Hawaii's ongoing Hepatitis A outbreak is now 168, according to the most recent update from the Hawaii State Department of Health. That is an increase of 23 new cases since the last update on Aug. 3.

HEPATITIS A- U.S. 2018



CDC - Accessed 11/2/2018

CLINICAL PRESENTATIONS

- Asymptomatic disease without jaundice
- Symptomatic, self-limiting disease with jaundice for less than 8 weeks
- Cholestatic jaundice lasting more than 10 weeks
- Relapsing acute hepatitis, with two or more instances over a 10-week period
- Acute hepatic failure

HEPATITIS B

- First new vaccine in more than 20 years approved by FDA
- **Heplisav-B (Dynavax)**
 - Contains CPG 1019 Adjuvant + 20 mcg Hepatitis Surface Antigen (recombinant)
 - Two doses effective in Immunocompetent Patients
 - Three dose regimen studied in those with CKD
- No data in HIV-Infected Persons

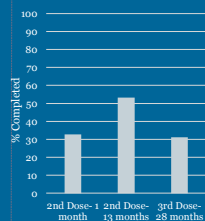
VACCINE ADHERENCE

- National Survey of Adults Receiving First HBV Vaccination
 - N= 535,759

- Completion of Vaccine Series Determined

RESULTS

- No significant difference by age group



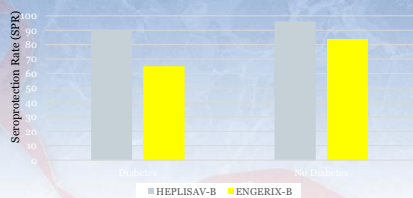
Tranham et al, VACCINE 2018

Efficacy endpoints-HEPLISAV-B FDA-approval

	HEPLISAV-B	Engerix-B	Difference in SPR (95% CI)	Difference in SPR % (95% CI)
HBV-10 (18-55)	85.0% (N=1,011)	81.2% (N=1,021)	3.7% (10.4, 17.8)	4.3%
HBV-16 (40-70)	90.1% (N=1,121)	70.5% (N=353)	19.6% (14.7, 24.8)	21.6%
HBV-23 (Dialysis)	90.0% (N=648)	65.1% (N=321)	24.9% (19.3, 30.7)	27.7%

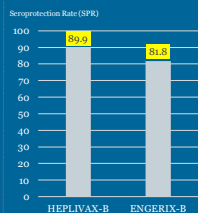
SPR= Seroprotection rate

HEPLISAV-B Diabetes Patients



HEPLISAV-B Dialysis Patients

- **Multicenter, randomized trial**
 - N= 507 vaccine and HBV exposure naïve
 - HEPLISAV-B 3 dose regimen vs. 4 doses Engerix-B 40 mcg (2 20 mcg shots)
 - Powered for non-inferiority, 10% margin
- **RESULTS**
 - Both non-inferiority and several secondary superiority measures met



Janssen RS et al. VACCINE, 2013

AUDIENCE RESPONSE QUESTION 2

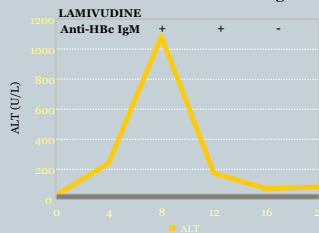
- A 52 yo man with HBV/HIV coinfection is seen in followup. He c/o increasing abdominal pain, nausea and vomiting. His urine has become dark in color. He reports unprotected sex with men and women.
- He was recently switched to a 2 drug regimen of dolutegravir/lamivudine from raltegravir/tenofovir/emtricitabine
- You are MOST concerned about....

AUDIENCE RESPONSE QUESTION 2...You are MOST concerned about....

1. Drug Hepatotoxicity
2. Acute HCV Infection
3. Acute renal failure
4. Hepatitis B flare
5. Hepatitis D Superinfection

HBV/HIV Coinfection

Lamivudine Breakthrough

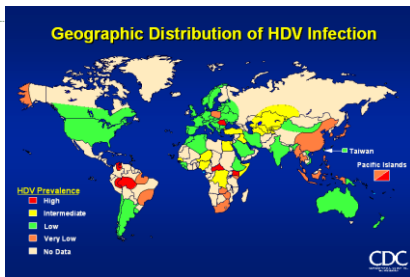


Bessesen et al., CID, 1999

HDV Significance

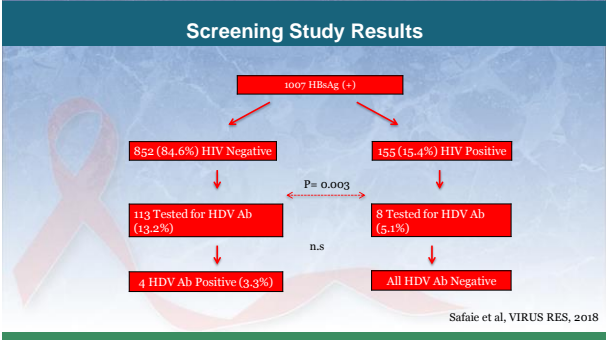
- HDV infection is associated with
 - Increased liver disease severity in setting of both superinfection and coinfection with HBV
 - More rapid rates of disease progression and early cirrhosis.
 - Increased risk of HCC (up to 3x fold in HBV-cirrhosis)

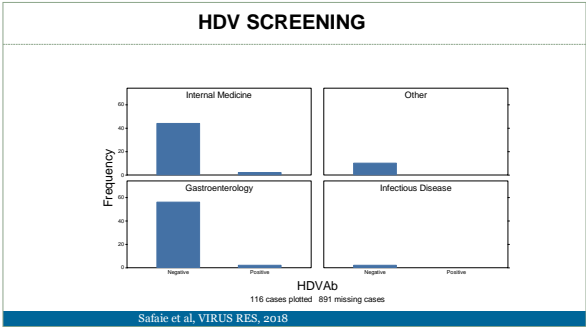
Geographic Distribution of HDV Infection

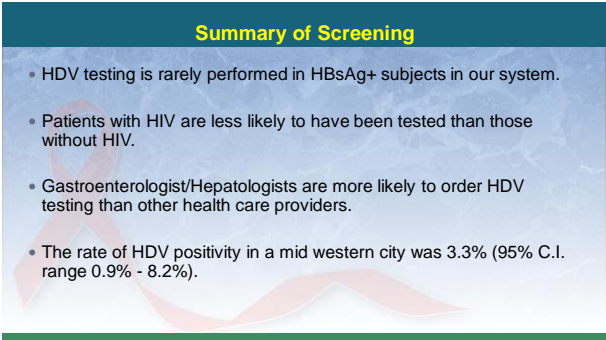


HDV TESTING RECOMMENDATIONS among HBsAg+ Individuals

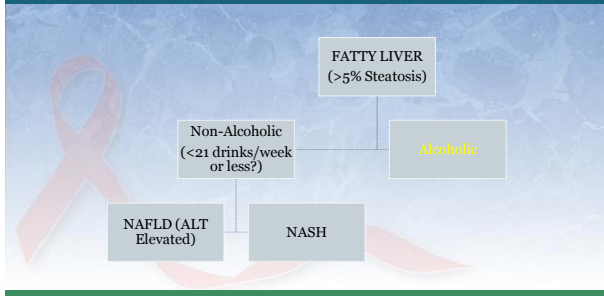
- **AASLD Guidelines:** "Laboratory tests should include assessment of liver disease, markers of HBV replication, and tests for coinfection with HCV, HDV, or HIV in those at risk" which includes all individuals from HDV endemic areas and those with history of IDU."
- **EASL Guidelines:** "Other causes of chronic liver disease should be systematically looked for including co-infections with HDV, HCV, and/or HIV (A1)"
- **APASL Guidelines:** "Other causes of chronic liver disease should be systematically looked for, including coinfections with HDV"



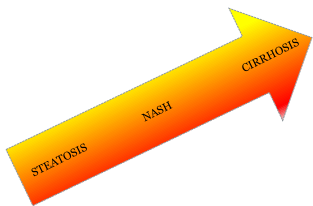




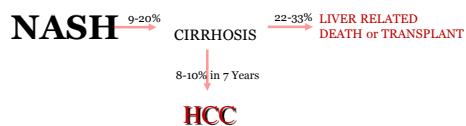
WHAT IS NAFLD?



FATTY LIVER A Continuum of Disease

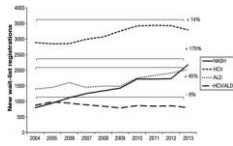


NATURAL HISTORY of NASH



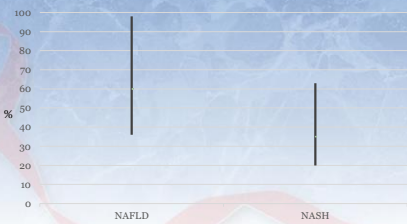
Adapted from Mishra A & Younossi ZM, J CLIN EXP HEPATOLOGY 2012

LIVER TRANSPLANTATION TRENDS NASH CIRRHOSIS



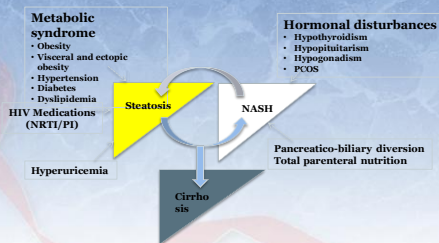
Carter D et al, CLIN LIVER DISEASE, 2017

NAFLD/NASH in HIV Prevalence



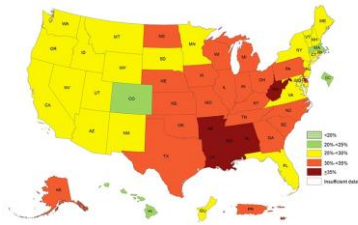
Lemstra et al, AIDS, 2006; Crum-Cianciola N et al, 2009, JAIDS; Ingillo P et al, HEPATOLOGY, 2009; Sterling R et al, J CLIN GASTRO, 2010; Moore et al, CVR, 2010; Viallet et al, ALIMENTARY PHARM THER, 2010

Risk Factors for NALFD in those with HIV



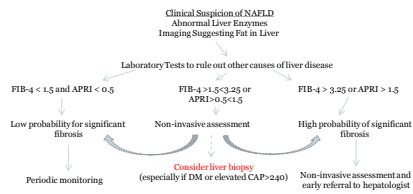
Sherman and Sterling in Zakim and Boyer, HEPATOLOGY 2017

OBESITY in U.S.



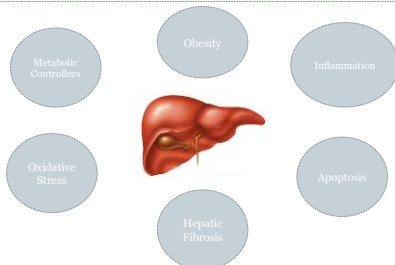
CDC, 2016

Diagnostic/Management Algorithm NAFLD in HIV



Sherman & Sterling in Zakim and Boyer, HEPATOLOGY, 2017

NAFLD/NASH TREATMENT TARGETS OF OPPORTUNITY



CONCLUSION

- Liver Disease remains an important consideration in those with or without HIV infection
- Viral infections that were rare have become common again
- Changes in cART management require awareness of coinfections
- NAFLD/NASH is a growing problem

Question-and-Answer

IAS-USA

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SUGGESTED READINGS

Bessesen M, Ives D, Condeay L, Lawrence S, Sherman KE. Chronic active hepatitis B exacerbations in human immunodeficiency virus-infected patients following development of resistance to or withdrawal of lamivudine. *Clin Infect Dis*. 1999;28(5):1032-1035.

Rossetti B, Montagnani F, De LA. Current and emerging two-drug approaches for HIV-1 therapy in ART-naive and ART-experienced, virologically suppressed patients. *Expert Opin Pharmacother*. 2018;19(7):713-738.

Safaie P, Razeghi S, Rouster SD, Privitera I, Sherman KE. Hepatitis D diagnostics: utilization and testing in the United States. *Virus Res*. 2018;250:114-117.

Sherman KE, Kottlil S. Hepatitis A and E. In: Schiff ER, Willis CM, Reddy KR, eds. *Schiff's Diseases of the Liver*. 12th ed. Wiley-Blackwell; 2018.