

HIV and Liver Disease

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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
- Be aware of real-time data regarding HCV treatment in HIV-infected persons
- Know when and how to screen for NAFLD/NASH

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ARS 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?

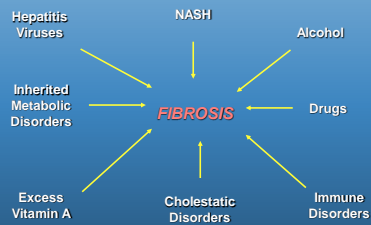
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ARS QUESTION 1: Which is of the following is most likely?

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

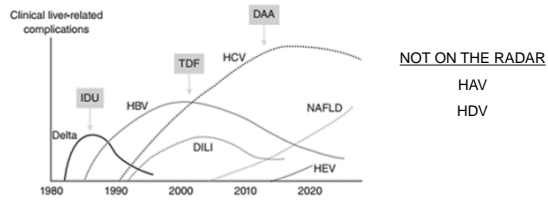
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CAUSES OF LIVER INJURY AND FIBROSIS



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EVOLUTION OF LIVER INJURY IN HIV



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Sherman KE et al, HEPATOLOGY COMM, 2017

TOPICS

- VIRAL HEPATITIS
 - Changing Epi and New Concerns
 - HBV New Vaccine
 - HCV Treatment in HIV-Infected Persons
- NAFLD/NASH
 - Increased Recognition
 - New Therapies?

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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

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Arkansas Officials Warn Of Another Possible Hepatitis A Exposure.

The AP (10/10/18) reports the Arkansas Department of Health is warning about another potential hepatitis A exposure in "an employee of Mandingos Callebaut in Jonesboro" who tested positive.

Multistate outbreak of hepatitis A linked to frozen strawberries: 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.

How do you answer growing food workers mean for you? Eight questions answered

Terry DeMio and Anne Saker, Cincinnati Enquirer Published 10:50 p.m. ET Updated 5:22 a.m. ET Sept. 5, 2018

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 AUBURN DISPATCHER | 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. It is an increase of 33 new cases since last update on Aug. 3.

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HEPATITIS A- U.S. 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

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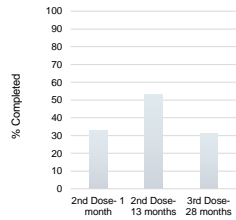
HEPATITIS B

- 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

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VACCINE ADHERENCE

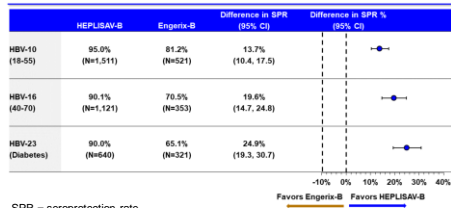
- National Survey of Adults Receiving First HBV Vaccination
 - N= 535,759
- Completion of Vaccine Series Determined
- RESULTS
 - No significant difference by age group



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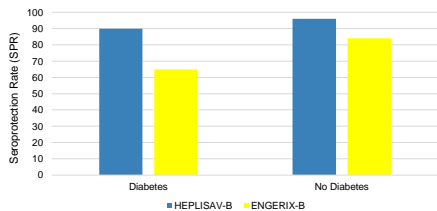
Tranham et al, VACCINE 2018

Efficacy endpoints-HEPLISAV-B FDA-approval



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HEPLISAV-B Diabetes Patients



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VRBPAC Briefing Document, 28 July 2017

ARS 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 dolutegrevir/lamivudine from raltegravir/tenofovir/emtricitabine

You are MOST concerned about....

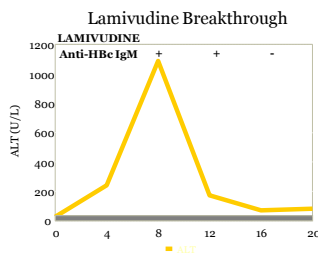
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ARS QUESTION 2: You are MOST concerned about....

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

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HBV/HIV Coinfection



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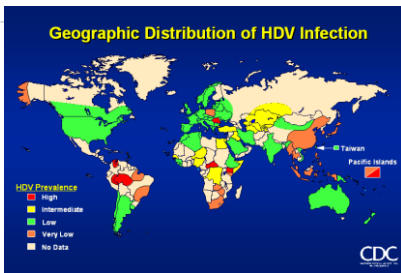
Bessesen et al., *CID*, 1999

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)

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Geographic Distribution of HDV Infection

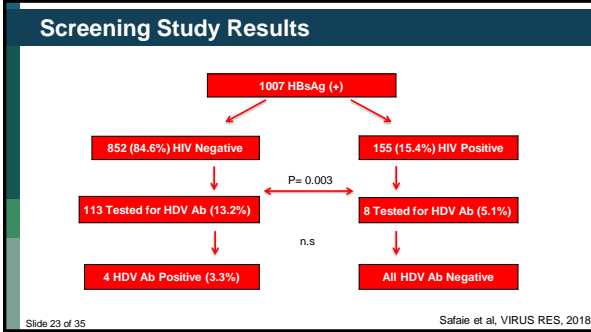


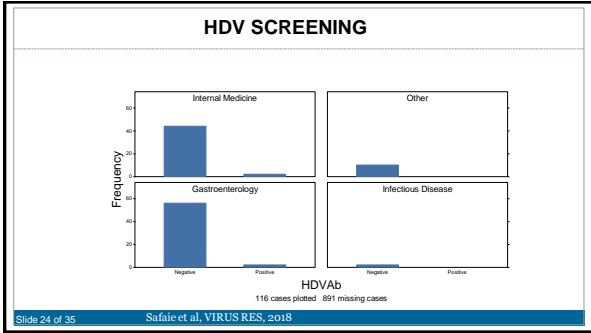
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HDV TESTING RECOMMENDATIONS among HBsAg+ Individuals

- **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

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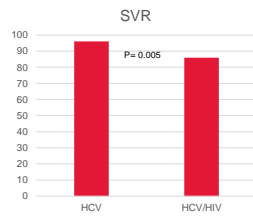




- ### Summary of Screening
- HDV testing is rarely performed in HBsAg+ subjects in our system.
 - Patients with HIV are less likely to have been tested than those without HIV.
 - Gastroenterologist/Hepatologists are more likely to order HDV testing than other health care providers.
 - The rate of HDV positivity in a mid western city was 3.3% (95% C.I. range 0.9% - 8.2%).
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HCV/HIV Treatment Real World Outcomes

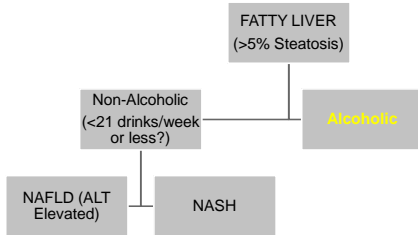
- HCV Treatment in NYC
- N= 350
 - 327 with complete datasets
 - HCV mono-infection= 253
 - HCV/HIV= 74
- Multiple DAA regimens used
- Duration- 12-24 weeks
- FACTORS ASSOCIATED WITH FAILURE in Univariate
 - Detectable HIV VL
 - Higher HCV VL
 - Lower CD4



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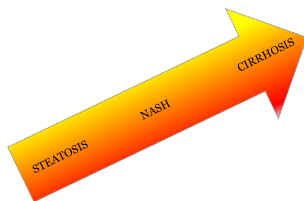
Gayam V et al, GUT Liver, 2018

WHAT IS NAFLD?



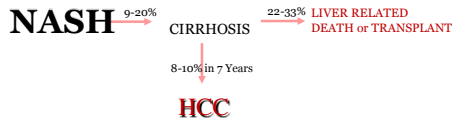
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FATTY LIVER A Continuum of Disease



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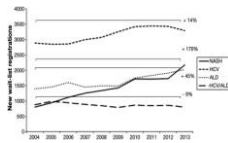
NATURAL HISTORY of NASH



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

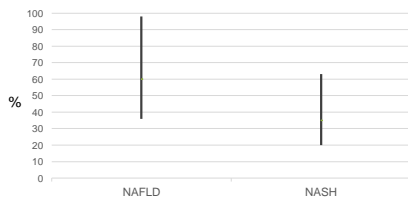
LIVER TRANSPLANTATION TRENDS NASH CIRRHOSIS



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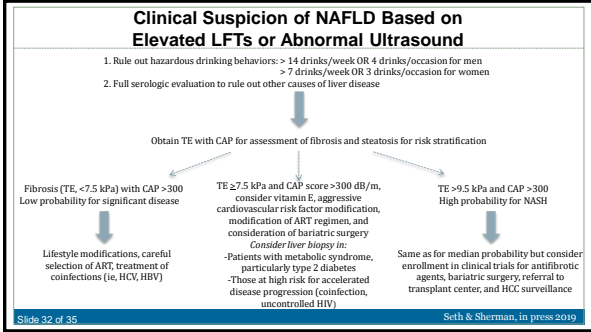
Carter D et al, CLIN LIVER DISEASE, 2017

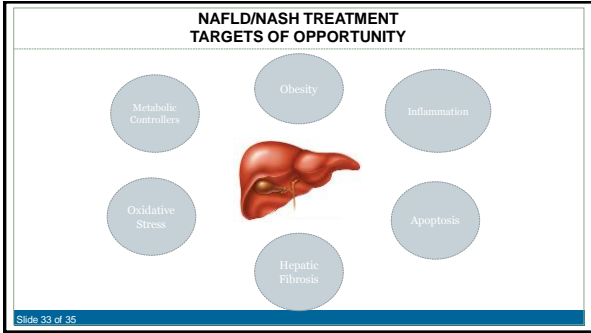
NAFLD/NASH IN HIV Prevalence



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Lemoine et al, AIDS, 2006; Crum-Clearforn, N et al, 2009, JAIDS; Ingiliz P et al, HEPATOLOGY, 2009; Sterling R et al, J CLIN GASTRO, 2013; Morise et al, CG CID, 2015; Vignati et al, ALIMENTARY PHARM THER, 2015





- ### 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
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Question-and-Answer

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