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 the following 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 AP (10/10/18) reports the Arkansas Department of Health is warning about another possible Hepatitis A exposure in "an employee of Murdocks Catfish in Jonesboro" who tested positive.

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

The U.S. Centers for Disease Control and Prevention (CDC) has found the outbreak on Friday afternoon to a total of 109 cases of Hepatitis A from eight states. Forty-seven of these individuals have been hospitalized, but no related deaths are being reported.

What do hepatitis A cases among food workers mean for you? Eight questions answered

Terry DeMio and Anne Sakai
Cincinnati Enquirer Published 10:50 p.m. ET Sept. 5, 2018

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

<table>
<thead>
<tr>
<th>National Survey of Adults Receiving First HBV Vaccination</th>
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<tbody>
<tr>
<td>N= 535,759</td>
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</tbody>
</table>

Completion of Vaccine Series Determined

RESULTS

- No significant difference by age group

Trantham et al, VACCINE 2018
Efficacy endpoints-HEPLISAV-B
FDA approval

<table>
<thead>
<tr>
<th></th>
<th>HEPLISAV-B</th>
<th>ENGERIX-B</th>
<th>Difference in SPR (%)</th>
<th>SPR 20% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV18 ( naive)</td>
<td>80.0%</td>
<td>76.0%</td>
<td>4.0%</td>
<td>(3.0, 5.0)</td>
</tr>
<tr>
<td>HBV12 (HIV)</td>
<td>91.3%</td>
<td>76.0%</td>
<td>15.3%</td>
<td>(14.1, 16.5)</td>
</tr>
<tr>
<td>HBV12 (Diabetes)</td>
<td>90.0%</td>
<td>76.0%</td>
<td>14.0%</td>
<td>(12.1, 15.9)</td>
</tr>
<tr>
<td>HBV12 (Dialysis)</td>
<td>90.0%</td>
<td>76.0%</td>
<td>14.0%</td>
<td>(12.1, 15.9)</td>
</tr>
</tbody>
</table>

SPR = Seroprotection rate

HEPLISAV-B
Diabetes Patients

Multicenter, randomized trial
- N= 507 vaccine and HBV exposure naive
- 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
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....

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

Bessen et al., CID, 1999

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HBV/HIV Coinfection

Lamivudine Breakthrough

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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)

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 for those at risk, which includes all individuals born in the years 1945 or earlier with symptoms of HDV."

- **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
Screening Study Results

- HBsAg (+): 852 (84.6%) HIV Negative
- 113 Tested for HDV Ab (13.2%)
- 155 (15.4%) HIV Positive
- 8 Tested for HDV Ab (5.1%)
- All HDV Ab Negative

P = 0.003 n.s

Safaie et al, VIRUS RES, 2018

HDV SCREENING

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%).
**WHAT IS NAFLD?**

- **FATTY LIVER**
  - (>5% Steatosis)
- **Non-Alcoholic**
  - (<21 drinks/week or less?)
- **NAFLD (ALT Elevated)**
- **NASH**

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**FATTY LIVER**

A Continuum of Disease

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**NATURAL HISTORY of NASH**

- **NASH**
  - 2-20%
- **CIRRHOSIS**
  - 22-33%
  - LIVER RELATED DEATH or TRANSPLANT
  - 8-10% in 7 Years
- **HCC**

Adapted from Mishra A & Younossi ZM, J CLIN EXP HEPATOLOGY 2012
LIVER TRANSPLANTATION TRENDS
NASH CIRRHOSIS

NAFLD/NASH IN HIV
Prevalence

Risk Factors for NALFD in those with HIV

Metabolic syndrome
- Obesity
- Visceral and ectopic obesity
- Hypertension
- Diabetes
- Dyslipidemia

HIV Medications (NRTI/PI)
- Pancreatic-biliary diversion
- Total parenteral nutrition

Hormonal disturbances
- Hypothyroidism
- Hypogonadism
- PCOS
- Hyperuricemia

Cirrhosis

Sherman and Sterling in Zakim and Boyer, HEPATOLOGY, 2017
OBESITY in U.S.

Diagnostic/Management Algorithm
NAFLD in HIV

Sherman & Steerling in Zakim and Boyer, HEPATOLOGY, 2017

NAFLD/NASH TREATMENT
TARGETS OF OPPORTUNITY

National Harbor, Maryland, December 9-11, 2018
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
SUGGESTED READINGS


