On the Liver Disease Front Lines: Hepatitis A, B and C Prevention and Treatment

Kurt Cook, MD, MSc

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein or of any evaluations or opinions expressed. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.

This CME session is supported by an educational grant to the AAFP from Gilead.

DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Kurt Cook, MD, MSc

Physician, Denver Health, Colorado; Assistant Professor of Family Medicine, Department of Family Medicine, University of Colorado School of Medicine, Denver.

Dr. Cook currently works with a largely Spanish-speaking patient population at Westwood Clinic, one of nine community health center sites that Denver Health maintains in neighborhoods throughout the city. He earned his medical degree from the University of Southern California (USC) School of Medicine, Los Angeles (now the Keck School of Medicine of USC), and completed a family medicine residency at North Colorado Medical Center, Greeley. He also earned a master’s degree in international health and tropical medicine and a Diploma in Tropical Medicine & Hygiene from the London School of Hygiene and Tropical Medicine, England. This training led to work in several areas related to infectious disease. For six years, he served as a county tuberculosis and sexually transmitted infection (STI) control officer and a physician in Ventura County, California, where he also oversaw the travel health clinic. Dr. Cook continues to pursue his interest in the interface between infectious diseases and family medicine through work on STI control at Denver Public Health and work on hepatitis B and C at Denver Health.

Learning Objectives

1. Follow current AAFP immunization schedules and preventive service recommendations for prevention of hepatitis infection.
2. Identify high-risk patients who should be screened for a hepatitis infection, and considered for hepatitis vaccination.
3. Counsel adult patients, and parents of children and adolescents, using available patient education resources and motivational interviewing about vaccine safety and efficacy.
4. Order appropriate laboratory and/or diagnostic tests to confirm diagnosis.
5. Construct an appropriate treatment plan for an adult patient with a confirmed diagnosis, taking into account tailoring of the treatment regimen for the individual, patient-specific barriers to treatment, follow-up monitoring, and making an appropriate referral.

Audience Engagement System

Step 1 Step 2 Step 3
Family medicine and the viral hepatitis “front lines”

- Prevention
- Screening
- Diagnosis
- Treatment
- Primary care of patients with chronic hepatitis B and C

Hepatitis A, B and C: Current incidence/prevalence (2015)

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>2800</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>22,000</td>
<td>~ 2.2 million</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>34,000</td>
<td>~ 3.5 million</td>
</tr>
</tbody>
</table>

Hepatitis A

- RNA hepatotropic virus
- Endemic in developing countries
- Acute viral hepatitis syndrome
- Self-limited illness
- Supportive care

Hepatitis A: Epidemiology

- Fecal-oral transmission: contaminated water or food
- Associated with travel to endemic areas
- Occasional food-borne outbreaks in US
  - 2013 contaminated pomegranate seed outbreak in SW US and Hawaii

AES Poll Question #1

- Hepatitis A vaccine is indicated for travel to which of the following areas:
  A. Africa
  B. China
  C. Western Europe
  D. A and B

Geographic Distribution of HAV Infection

http://virology-online.com/viruses/HepatitisA.htm
Hepatitis A: Diagnosis
- Acute hepatitis syndrome: symptoms, elevated AST/ALT/bilirubin
- History of travel to endemic area or other risk factors (MSM, contact, outbreak)
- Average incubation period: 28 days
- Serology: positive anti-HAV IgM

Acute Hepatitis A: Treatment
- Supportive care
- Self-limited illness
- Resolution usual in 2 to 3 months
- Report to health department
- Care of contacts

Hepatitis A: Prevention
- Identify patients at-risk or exposed
  - Travelers, MSM, exposed in outbreak, household contacts, chronic liver disease
- Vaccination as primary preventive measure and post-exposure
- Hepatitis A IgG post-exposure

Hepatitis A: Vaccination
- Adult vaccination rates low
  - 16% of travelers to endemic areas
  - 14% of patients with chronic liver disease
- Increase use of patient education and motivational interviewing to increase rates

95% decline in rates of hepatitis A since vaccine introduced in 1995
### Hepatitis B
- Hepatotropic DNA virus
- Blood borne transmission
- Acute and chronic viral hepatitis
- Global public health problem, especially Asia and Africa
- Up to 2.2 million chronic HBV patients in US
- Sequelae: cirrhosis, liver failure and HCC

### Hepatitis B: Epidemiology
- Blood-borne viral infection
- Mother-to-infant transmission common globally in Asia and Africa
- IVDA, sexual transmission and other blood exposure more common in US

### AES Poll Question #2
- Which of the following individuals has the highest likelihood of developing chronic HBV infection?
  A. 33 y/o female infected via IV drug use.
  B. Infant of HBsAg positive mother infected at birth and untreated.
  C. 46 y/o health worker infected by needle stick injury.

### Hepatitis B: Epidemiology
- Risk of developing chronic HBV
  - 90% of acutely HBV-infected infants
  - 5% of acutely HBV-infected adults
  - Viral load of source case also important

### Hepatitis B: Screening
- Screen at-risk groups for HBsAg
  - Born in Asia or Africa
  - Parents born in Asia or Africa (perinatal transmission)
  - IVDU
  - Pregnant women
  - STD exposure
  - HCV and HIV infected
Hepatitis B: Diagnosis

• Acute HBV
  – Acute hepatitis syndrome
  – Risk factors
  – Serology: positive HBsAg and anti HBc IgM

Hepatitis B: Diagnosis

• Chronic HBV
  – Symptoms variable: none to advanced liver disease
  – Risk factors
  – Serology: positive HBsAg
  – HBV DNA viral load, HBeAg, ALT important for treatment decision-making

Chronic Hepatitis B: Pathophysiology

• Chronic, dynamic infection
• Chronic hepatic inflammation leads to fibrosis/cirrhosis
• 25% of patients with chronic HBV die prematurely of cirrhosis or hepatocellular carcinoma (HCC)

AES Poll Question #3

• Which of the following is not a goal of treatment of chronic HBV infection?
  A. Elimination of the virus.
  B. Decreased levels of viremia.
  C. Decreased risk of development of HCC.
  D. Improvement in levels of ALT and hepatic inflammation.

Hepatitis B: Treatment

• High levels of viremia associated with liver damage
• Viral suppression: improved outcome
• Goals of treatment: suppression of virus replication; decreased liver inflammation and fibrosis
• Chronic HBV not yet curable; soon?

Hepatitis B: Treatment

• Factors in decision to initiate antiviral therapy:
  – Presence of cirrhosis
  – HBV DNA viral load
  – ALT level
  – Pregnancy
Hepatitis B: Treatment
• Antiviral therapies
  – Pegylated interferon
  – Entecavir
  – Tenofovir
  – Others

Hepatitis B: Pregnancy
• Screen pregnant women for HBsAg
• Check HBV viral load at 28 wks in HBsAg positive women
• Treat with tenofovir if HBV DNA >2x10⁵ IU/ml
• Newborns with HBsAg positive mother get HBV vaccine and HBIG at birth

Hepatitis B: Prevention
• Vaccination
  – Recombinant vaccine since 1985
  – Contains 95% HBsAg protein
  – Over 90% recipients develop adequate immunity with 3 vaccine series

Hepatitis B: Prevention
• Vaccination schedule
  – Infant: birth, 1-2 mos, 6-18 mos
  – Children: by 11-12 if not as infant
  – Adults: 3-dose series if at-risk:
    • STD risk
    • ESRD/dialysis
    • HIV or HCV infection or other chronic liver disease
    • Occupational risk

Hepatitis B: Vaccination
• Adult vaccination rates low
  – 30% of patients with chronic liver disease
  – 60% of health care providers
• Increase use of patient education and motivational interviewing to increase rates

www.cdc.gov
Hepatitis C
- Hepatotropic RNA virus
- 6 genotypes; type 1 most common in US
- Blood-borne transmission
- Acute and chronic viral hepatitis
- 3.5 million chronic HCV patients in US
- Cirrhosis, liver failure and HCC

Hepatitis C: Epidemiology
- Blood-borne viral infection
- ~85% develop chronic infection
- IVDA
- Blood product infection prior to screening
- ESRD/dialysis
- Multiple sex partners

Hepatitis C: Epidemiology
- High rates of HCV transmission in 1960’s and 1970’s
  - Current increasing rates of liver disease due to chronic HCV in “baby boomer” generation

Hepatitis C: Screening
- Risk-based screening
  - Injection drug use
  - Transfusions/blood products prior to screening
  - Dialysis patients
  - Intimate contact with person with HCV
  - HIV positive
  - Elevated LFTs
  - Occupational exposure

Hepatitis C: Screening
- Limitations of risk-based screening strategy
  - Lack of provider awareness of screening recommendations
  - Only 25% of HCV positive patients would have reported risk factors and been screened

Hepatitis C incidence in US
www.hepatitiscuw.edu
Hepatitis C: Screening
- Birth cohort HCV screening (CDC recommendation, 2012)
  - All persons born 1945-1965: one-time HCV testing
  - 75% of current chronic HCV in this age cohort

Hepatitis C: Diagnosis
- Acute HCV
  - Acute hepatitis syndrome
  - Positive HCV antibody
  - Positive HCV RNA

Chronic Hepatitis C: Diagnosis
- Symptoms and signs: variable; none to advanced liver disease
- Serology:
  - Positive HCV antibody
  - Positive HCV RNA

AES Poll Question #4
- Approximately 85% of persons infected with HCV will develop chronic infection. Of these, what percentage develop cirrhosis without treatment?
  A. Nearly 100%
  B. 50%
  C. Less than 5%
  D. 20-30%

Chronic HCV: Pathophysiology
- Chronic HCV causes variable degrees of chronic hepatocellular inflammation and progressive fibrosis
- ~85% HCV infected develop chronic infection
- ~20-30% chronic HCV develop cirrhosis
Hepatitis C: Treatment

- Direct acting antivirals (DAA)
  - Interferon-free regimens
  - All oral
  - Well-tolerated
  - Usually 12 weeks of therapy
  - High rates of SVR (sustained virologic response):
    >90% in almost all subgroups
  - GI side effects, headache common but tolerable

Hepatitis C: Treatment Type 1

- Elbasvir-grazoprevir (Zepatier)
- Ledipasvir-sofosbuvir (Harvoni)
- Ombitasvir-paritaprevir-ritonavir (Technivie) plus dasabuvir
- Sofosbuvir-velpatasvir (Epclusa)
- Declatasvir (Daklinza) plus sofosbuvir

Case

- CS is 64 yr old male with DM, obesity, chronic HCV and history of EtOH abuse
  - Baseline labs: ALT 329, Alb 3.4, T bili 1.3, INR 1.0, A1C 7.4, HCV DNA 8,000,000, HCV genotype 1a
  - Imaging: CT liver nodularity, splenomegaly
  - FIB-4: greater than 3.25 (high probability of cirrhosis)

- Treatment: Zepatier x 12 weeks
- Pt tolerated treatment well: mild HA, loose stools
- Post-treatment labs:
  - ALT 30, T bili 1.0, HCV DNA undetectable
Chronic HBV and HCV: Pathophysiology

- Factors that accelerate fibrosis/cirrhosis:
  - Alcohol
  - Hepatic steatosis
  - Concurrent infection: HIV, HBV/HCV
- Development of hepatocellular carcinoma (HCC): risk HBV > HCV

Chronic HBV and HCV: Assessment of liver fibrosis/cirrhosis

- Liver biopsy: gold standard, invasive, inaccurate in 20% of cases
- APRI score
- FIB-4
- FibroSure

Chronic HBV and HCV: Assessment of fibrosis/cirrhosis

- Ultrasound, CT, MRI: variable accuracy
- Transient elastography
  - Ultrasound
  - Measure of liver "stiffness"
  - Correlates with degree of fibrosis

Chronic HBV and HCV: Hepatocellular carcinoma

- Chronic HBV and HCV increase risk for HCC
- HCC risk HBV > HCV
- HCC screening in chronic HBV and HCV may be associated with improved outcome
HCC screening
• HCC detected due to symptoms has very poor prognosis: 5 yr survival 0-10%
• Single large prospective study from China in patients with chronic HBV showed survival benefit with screening
• No large study of screening in chronic HCV

HCC screening/surveillance
• Liver US currently recommended screening modality for detection of HCC
• Screening US in chronic HBV with or without cirrhosis each 6 months
• Screening US in chronic HCV with cirrhosis each 6 months

Practice Recommendations
• Identify patients in your practice with risk factors for HAV, HBV and HCV and vaccinate those at-risk
• Implement birth cohort “baby boomer” HCV screening
• Partner with specialty colleagues to promote treatment of chronic HBV and HCV

On-line Resources
• [https://www.cdc.gov/hepatitis/index.htm](https://www.cdc.gov/hepatitis/index.htm) – CDC viral hepatitis website
• [http://www.hepatitisc.uw.edu/](http://www.hepatitisc.uw.edu/) – Free online hepatitis C modules by University of Washington
Questions

Contact Information

• Kurt Cook, MD
• kurt.cook@dhha.org
• 720-250-8393