Welcome to Liver Disease ECHO

This project is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided from the HHS Secretary's Minority HIV/AIDS Fund.

WHAT WE DO

- We're accepting **case presentations and questions pertaining to:**
  - Elevated Liver Function Tests
  - Cirrhosis
  - Managing Complications of Decompensated Cirrhosis – Ascites, encephalopathy, esophageal varices
  - Alcohol-related liver disease, including Alcohol Hepatitis
  - Autoimmune liver disease – Autoimmune Hepatitis, Primary Biliary Cholangitis, Overlap
  - Nonalcoholic fatty liver disease/Nonalcoholic steatohepatitis
  - Hepatocellular carcinoma
- Provide Expert Panelists
- Didactic Presentations pertaining to ECHO topics

CONSULTANT TEAM

- Brian McMahon, MD Hepatologist
- Youssef Barbour, MD Hepatologist
- Lisa Townshend, ANP Hepatology Provider
- Annette Hewitt, ANP Hepatology Provider
- Leah Besh, PA-C HIV/Hepatology Provider
- Anne Fleetwood, MS, RDN, NDN
- Brittany Keener, PharmD, MPH, BCPS
- Lucia Neander, PhD Clinical Psychologist

AK LIVER DISEASE ECHO – CONTINUING EDUCATION

Approved Provider Statements:

Alaska Native Tribal Health Consortium (ANTHC) is accredited by the Washington State Medical Association to provide continuing medical education for physicians.

ANTHC is approved as a provider of nursing continuing professional development by the Montana Nurses Association, an accredited approver with distinction by the American Nurses Credentialing Center's Commission on Accreditation.

Contact Hours:

ANTHC designates this live activity for a maximum 12 *AMA PRA Category 1 Credit(s)* ™ for the entire series. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ANTHC designates this activity as meeting the criteria for one nursing contact hour credit for each hour of participation up to a maximum 12 hour(s), including 6 total pharmacotherapeutics (Rx) contact hours for the entire series.

1 Contact hours, including 0.5 Rx contact hours, or 1 AMA PRA Category 1 Credit(s) ™ awarded per sessions attended.

Conflict of Interest Disclosures:

Lisa Townshend-Bulson, faculty for this educational event, is the primary investigator in a study funded in part by Gilead Sciences; Anne Fleetwood, faculty for this educational event, is a contractor with Tandem Diabetes Care. All of the relevant financial relationships listed for these individuals have been mitigated.

Requirements for Successful Completion:

To receive CE credit please make sure you have actively engaged in the entire activity, your attendance is recorded by the facilitator, and complete the course evaluation form found here: https://forms.gle/R8vibUZgMbRcoScw9.

For more information contact
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ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

TODAY'S PRESENTER- DR. BRIAN MCMAHON

Dr. McMahon has been the Program Director of the Liver Disease and Hepatitis Program since 1983. He currently serves as the Scientific Program and Clinical Director. He has practiced medicine in Alaska for over 40 years.

Dr. McMahon has been the Principal Investigator on a majority of Liver Disease and Hepatitis Program's funded research projects.

He has authored or co-authored over 150 peer-reviewed publications on viral hepatitis and liver disease, and is a widely recognized expert in hepatology.

Dr. McMahon is a coauthor of the American Association for the Study of Liver Disease, Hepatitis B Practice Guidelines.

EVALUATION OF ABNORMAL LIVER FUNCTION TESTS

Brian J McMahon MD

Liver Disease and Hepatitis Program

Alaska Native Tribal Health Consortium

CONFLICTS OF INTEREST

- None

ONE OF THE FOLLOWING STATEMENTS IS FALSE

A. 8% of Americans will have one or more abnormal Liver Function test (LFT)
B. NAFLD (or MAFLD) is the number one etiology for an abnormal LFT in clinical practice
C. HIV is the number one chronic infectious disease cause of death in the USA
D. The Audit C Questionnaire should be given to persons seen in every clinic
E. The best screening test for hemochromatosis is an iron saturation

PROPERTIES OF THE LIVER: A REMARKABLE ORGAN

- Replacement of liver occurs 3-4 times/lifetime in normal persons
- Complete liver regeneration occurs in few months after ½ liver is removed surgically
- In person with chronic hepatitis total liver hepatocyte replacement every 4-6 months
- Scarring in the liver is reversible, even in persons with early cirrhosis
- Liver Disease is the number sixth or seventh leading cause of death for Alaska Native/American Indian People as opposed the tenth leading cause in the US population as a whole

THREE TYPES OF LIVER FUNCTION TESTS

- Cholestatic liver enzymes
- Hepatocellular liver enzymes
- Tests of liver synthetic function

LIVER FUNCTION TESTS: CHOLESTATIC ENZYMES

- Alkaline Phosphatase:
  - Located in biliary epithelium but also bone and lung;
  - Fractionation differentiates liver and other organs
- Gamma Glutamyl Transpeptidase (GGTP):
  - Located in bile epithelium
  - Enzyme induced by multiple drugs/alcohol

PATTERNS OF ABNORMAL LFT'S: CHOLESTASIS

- Predominant Elevation of Alkaline Phosphatase (>3:1 ratio Alk Phos: ALT
  - Confirmation with elevation of GGTP or 5 ' Nucleotides
  - Normal or minimally elevated transaminases
  - Total Bilirubin may be elevated
- Isolated elevation of Bilirubin
  - Inherited: Gilbert's most likely

LIVER FUNCTION TESTS: AMINOTRANSFERASE

- Hepatocellular
  - ALT (SGPT): Cytosol enzyme, located near cell membrane, primarily a hepatic enzyme
  - AST (SGOT): Located near mitochondria. Found in many other organs
  - LDH: Nonspecific, found in many other organs, only helpful in ischemic hepatitis where it is disproportionately higher than ALT

NORMAL LIMITS FOR AMINOTRANSFERASE ALT

- Normal range differs from lab to lab:
- Upper limit of normal laboratory ranges (30 U/L to 72 U/L)
  - Probable Upper limit of normal range
    - Men: ~30-35 U/L
    - Women: ~20-25 U/L
    - Anything above 40 U/L is certainly abnormal

PATTERNS OF ABNORMAL LFT'S: HEPATOCELLULAR

- Predominant Elevation of ALT and AST
- Normal or Minimal Elevation of Alkaline Phosphatase

TESTS OF LIVER SYNTHETIC FUNCTION

- Biochemical products synthesized in or metabolized by liver; These tests are abnormal when liver is failing
  - Albumin
  - Prothrombin Time (INR)
  - Bilirubin
    - Direct: conjugated
    - Indirect: unconjugated
      - Gilberts syndrome: benign elevation of unconjugated bilirubin

ACUTE AND CHRONIC HEPATITIS: DEFINITIONS

- Acute Hepatitis
  - Elevated aminotransferase levels (ALT/AST) > 10 times upper limit of normal
  - May or may not be associated with Jaundice
- Chronic Liver Disease
  - Chronic Hepatitis:
    - ALT and/or AST above upper limit of normal on at least two occasions 3 months apart
  - Chronic liver disease:
    - Meets definition of chronic hepatitis or alkaline phosphatase or GGT elevated on at least two occasions 3 months apart

MAGNITUDE OF AST AND ALT ELEVATIONS: VARIATIONS IN LEVELS OF ALT AND AST

- ●**Alcoholic fatty liver disease**: AST <8 times the upper limit of normal; ALT <5 times the upper limit of normal. AST>ALT
- ●**Nonalcoholic fatty liver disease**: AST and ALT <4 times the upper limit of normal.
- ●**Acute viral hepatitis or toxin-related hepatitis with jaundice**: AST and ALT >25 times the upper limit of normal.
- ●**Ischemic hepatitis (ischemic hepatopathy, shock liver, hypoxic hepatitis):** AST and ALT >50 times the upper limit of normal (in addition the lactate dehydrogenase is often markedly elevated).
- ●**Chronic hepatitis C virus infection**: Wide variability, typically normal to less than twice the upper limit of normal, rarely more than 10 times the upper limit of normal.
- ●**Chronic hepatitis B virus infection**: Levels vary; the AST and ALT may be normal in inactive carriers, whereas patients with chronic hepatitis B may have mild to moderate elevations which can fluctuate over time; with exacerbations, levels are more than 10 times the upper limit of normal. Approximately a third of patients with chronic hepatitis B may also have NAFLD

ACUTE HEPATITIS B: ETIOLOGIES

- Hepatitis viruses: A, B, C, D and E
- Other viruses: CMV, EBV, others
- Parasites: Toxoplasmosis
- Rickettsia: Psittacosis
- Alcoholic hepatitis: AST> ALT
- Acetaminophen hepatitis: Can with alcohol with as low as 2gms/day
- Acute hepatitis due to Drug Induced Liver Injury (DILI)
- Ischemic hepatitis (e.g. with shock): LDH > ALT
- Medications including herbal medications/OTC drugs
- Autoimmune hepatitis

ACUTE HEPATITIS: LABORATORY EVALUATION

- Liver Function: ALT, AST, Bilirubin (Direct and Total), Alkaline Phosphatase, Prothombin time (INR)
- Diagnostic tests: anti-HAV IgM, anti-HBc IGM, HBsAg (if positive do anti-HDV) anti- HCV (if negative and risk factors do HCV RNA), anti-HEV if travel to endemic area and above tests negative
- If above negative: CMV IgM, EBV profile, Toxoplasmosis IgM, ANA, smooth muscle antibody and IgG in women

CHRONIC HEPATITIS

- Definition: ALT and/or AST elevated on two occasions at least 3 months apart
  - In > 30% of persons with one abnormal LFT, the test will have returned to normal on retesting 3 weeks later (Ann Intern Med 2008;148:348-352)
  - Many things can elevate ALT or AST
    - Acute viral illness like influenza
    - Vigorous exercise
    - A few dose of common medications such as ibuprofen (NSAID)

PREVALENCE OF ABNORMAL ALT OR AST IN US POPULATION: NHANES III

- 15,676 persons ≥ 17 years old
- 7.9% abnormal ALT (>40 U/L men, 31 U/L women) or AST (>37 U/L men, 31 U/L women);
  - 9.3% of men, 6.6% of women
- 69% ALT/AST elevation unexplained
  - Not due to HBV, HCV, Alcohol or iron
  - Strong association to presence of metabolic syndrome: ↑ BMI, ↑ waist circumference, ↑ triglycerides, ↑ fasting insulin, type 2 DM, HTN, ↓ HDL

Am J Gastroenterology 2003;98:960-7

MOST COMMON ETIOLOGIES OF ABNORMAL LFTS: MOST COMMON

- Non-Alcoholic Fatty Liver Disease (NAFLD);
  - Most common cause in US and Europe
  - May occur in 15%-25% of US population
- Alcohol use: Audit-C
- Medications
- Hepatitis C (1.8% of the population)
- Hepatitis B: 0.3% of population but ~ 10% of persons emigrating from endemic countries
- Hemochromatosis: 1/300-400 Caucasians

LESS COMMON ETIOLOGIES OF ABNORMAL LFTS

- Autoimmune liver diseases
  - Autoimmune Hepatitis (females>males)
  - Primary Biliary Cholangitis (females>males)
  - Primary Sclerosing Cholangitis (males>females)
- Wilson's Disease
- Alpha 1 Anti-trypsin Deficiency
- Other genetic and metabolic conditions
- Biliary obstruction, metastatic cancer
- Any acute illness (influenza)

LACK OF AWARENESS AND ASSOCIATED DEATHS DUE TO LIVER DISEASE IN US

Virus	Prevalence	% of Population Unaware of liver abnormality	Deaths in 2006 Related to Infection
HBV	800,000 –1.4 million	About 65%	3,000
HCV	2.7–3.9 million	About 75%	12,000
HIV	1.1 million	About 21%	14,016
NAFLD	One hundred million plus	75%	

LABORATORY TESTING APPROACH TO PERSONS WITH ELEVATED LIVER TRANSAMINASES

- History:
  - Risk factors for viral hepatitis
  - Family history of liver disease: what type?
  - Recent Travel
  - Pets
  - Any medications including OTC, herbals and illicit drugs
  - Risk factors for metabolic syndrome
  - Alcohol history
- After H&P consider repeating in 2-3 months if no evidence of liver disease is present

LIVER DISEASES YOU DON'T WANT TO MISS: WE WILL COVER THESE DISEASES IN LATER ECHOS

- Autoimmune Liver Diseases
  - Autoimmune hepatitis (AIH): ANA, Actin Smooth Muscle antibody, IgG
  - Primary Biliary Cholangitis (PBC) Anti mitochondrial antibody
  - Primary Sclerosing Cholangitis (PSC): MRCP
- Hemochromatosis: Iron saturation
- Wilsons Disease: serum ceruloplasmin
- Chronic Viral Hepatitis: test for antibody to hepatitis C and HBsAg
- Alcohol associated liver disease: Audit C Questionnaire

LABORATORY TESTS

- On all persons: Viral Hepatitis serology: HCV antibody, HBsAg, hep B core antibody and surface antibody, hepatitis A antibody IgM if acute
- On persons with Obesity or Metabolic Syndrome: Tests for the metabolic syndrome; Lipid panel, Hg AIC, fasting glucose, BP
- If viral serology negative and female or if male and personal or family history of any autoimmune disorder, do autoimmune liver disease workup
  - ANA, Actin smooth muscle antibody, IgG, Anti-mitochondrial antibody (AMA) IgM
- On Caucasian persons or persons without alcohol use disorder: Iron saturation: abnormal >40% men, >50% women
  - If elevated next check ferritin: if >1,000 due hemochromatosis genetic markers
- If all above are negative, consider ceruloplasmin if under age 40 and alpha-1-antitrypsin level if family history or evidence of chronic lung disease

SHOULD SCREENING FOR LIVER DISEASE BE A ROUTINE PART OF MEDICAL PRACTICE

- Who to Screen
  - All adults ages 18 through 79 for hepatitis C antibody one time: new CDC and USHSTF 2020 recommendation. Medicaid will reimburse for this.
    - Yearly screening for those with risk factors
    - HCV antibody positive: order PCR for HCV RNA
  - 30% plus persons with obesity (BMI<30, (pre) diabetes, Sleep Apnea, dyslipidemia for NAFLD with LFTs, FIB4, APRI, NAFLD fibrosis marker
    - If all these are WNL, repeat every 2-3 years
    - If LFTs are elevated or serologic markers suggest advanced fibrosis or cirrhosis, consider VCTE or equivalent or MRI elastography
  - Hepatitis B: All persons who were born outside US except Canada, Mexico, Japan and Western Europe
    - CDC is considering a recommendation for one-time adult universal screening and vaccination
  - Alcohol Associated Liver Disease: Audit-C test in all patients at each visit
  - Hemochromatosis: Controversial if Caucasian persons should have an iron saturation around age 40 to 50

CONCLUSIONS

- When screening laboratory panels are ordered, one or more abnormal LFT are frequent findings, especially using the accepted normal cutoff levels
- In those persons with abnormal LFT results it is important to screen those persons for treatable liver diseases
- Identifying treatable liver diseases can result in lowering mortality for AN/AI persons and correcting this disparity

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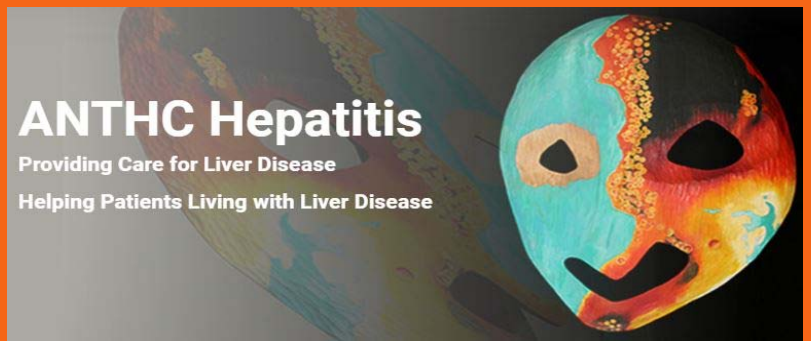
E. The best screening test for hemochromatosis is an iron saturation

LIVER DISEASE ECHO SCHEDULE AT A GLANCE

- March 18th Evaluating Abnormal Liver Function Tests – Brian McMahon, MD
- April 15th Noninvasive Markers for Liver Fibrosis – Brian McMahon, MD
- May 21st Management of Ascites – Youssef Barbour, MD
- June 17th Motivational Interviewing – Lucia Neander, PhD
- July 15th Nutrition for the Liver – Anne Fleetwood, MS, RDN, CDCES
- August 19th Drug Induced Liver Injury – Brittney Keener, MPH, BCPS

ADDITIONAL LEARNING OPPORTUNITIES

- ANTHC ID ECHO: HCV, HIV, PrEP, STIs,
  - The 2nd Tuesday of every month from 12:00-1:00PM Alaska Standard Time
    - 1CE/CME offered per session
  - anthc.org/project-echo/hcv-hiv-prep-stis-echo
- LiverConnect Webinar Program
  - Second Tuesday of every month 8:00-9:00AM Alaska Standard Time
    - Full Hour didactic topics on Liver Disease and related topics 1CE/CME offered
  - anthc.org/what-we-do/clinical-and-research-services/hep/liverconnect/



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Thank you!

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