“Ask the Experts”
Patient Education Program
All Presentations Combined
March 24, 2016
Hepatitis C
Non-alcoholic Fatty Liver Disease
Cirrhosis
Liver Wellness

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Hepatitis C
Goal for Today?

Knowledge About Hep C and the Liver

What is Hepatitis?

The word "hepatitis" means inflammation of the liver. Chemical exposure, certain drugs, some diseases, heavy alcohol use, bacterial and viral infections can all cause hepatitis.
Hep C

• RNA virus
• Formerly known as ‘non A, non B’ or transfusion associated hepatitis
• Virus isolated and named in the late 1980’s
• Unlike Hep A and B, there is no vaccine!!

Hep C: How Does One Acquire It?

• Blood to Blood transmission only
• Rare sexual transmission
• Blood transfusion, needle sharing, tattoo, intranasal cocaine

Hepatitis C Is Often Undiagnosed

• Despite its high prevalence, HCV often remains undiagnosed

More than three fourths of those with hepatitis C are undiagnosed
Screening: HCV

CDC (2012) recommending that everyone born during 1945 through 1965, also known as baby boomers, get a blood test for Hepatitis C. This recommendation calls for one-time testing of baby boomers.

Who Should Be Screened: HCV

The prevalence of anti-HCV among persons born during 1945–1965 is 3.23% (3), five times higher than among adults born in other years. The high prevalence of HCV among persons in this birth cohort reflects the substantial number of incident infections throughout the 1970s and 1980s and the persistence of HCV as a chronic infection. Males in this cohort had almost twice the prevalence as their female counterparts; HCV infection prevalence was highest among non-Hispanic black males (8.12%), followed by non-Hispanic white males (4.05%) and Mexican-American males (3.41%).

CDC:Recommendations and Reports
August 17, 2012 / 61(RR04)L-18
HCV: DIAGNOSTICS

- First line test is HCV Antibody
- If positive, order HCV PCR RNA and HCV Genotype

HCV Genotypes in US

- Hepatitis C virus
  - RNA virus - high mutation rates
  - Evolved different genotypes
- 6 known genotypes
  - Genotype 1 (75%)
  - Genotype 2 (6%)
  - Genotype 3 (10%)
  - Genotype 4-6 (10%)
- Genotypes 1-5 are the most common in the United States
- Little difference in mode of transmission or natural history of infection among different genotypes
- Predicts treatment response and may help to determine treatment duration

Why Important to Screen??

- Distribution of HCV Genotypes
  - Genotype 1: 75%
  - Genotype 2: 10%
  - Genotype 3: 10%
  - Genotype 4-6: 5%
Inflammation from Hep C in the Liver over Time Causes Scarring (Fibrosis). When there is More Scar Tissue than Healthy Tissue = Cirrhosis

Liver Cancer Has the Fastest Growing Death Rate in the US

Trends in US Cancer Mortality Rates

All Cancers (Average)

Uterus

Lung and Bronchus (Females)

Pancreas

Esophagus

Thyroid

Liver

Annual Percent Change (1996-2005)*

*Represents the annual percent change over the time interval
The Good News

HEPATITIS C CAN BE CURED!

Chance of clearing the virus with treatment depends on genotype, stage of disease and compliance with treatment regimen.

Hepatitis C

- New Oral Treatment Regimens
- Cure Rates Above 90% For Most
- Curing HCV Stops Disease Progression and Ongoing Scarring of Liver
- Well Tolerated
- Patients with Cirrhosis Will Still Need Lifelong Surveillance Even if Cured.
Non-Alcoholic Fatty Liver Disease (NAFLD)

- Spectrum of conditions associated with fatty deposition (steatosis) in liver cells
- Broadly subdivided into 2 categories:
  1. Non-Alcoholic Fatty Liver (NAFL): Simple steatosis
  2. Non-Alcoholic SteatoHepatitis (NASH): Steatosis with inflammation and liver cells injury with or without fibrosis (scarring)
- Diagnostic of exclusion

Non-Alcoholic Fatty Liver Disease (NAFLD) Spectrum

- **NAFL**: Lower risk of progression to cirrhosis
- **NASH**: More advanced phenotype with substantial risk of progression to cirrhosis


Non-Alcoholic Fatty Liver Disease (NAFLD)

- Increasingly prevalent
- “Silent” Disease
- Can be severe (NASH)
- No specific FDA-approved therapies

Rising Prevalence of NAFLD in the US (NHANES data)

Younossi Z et al. Clin Gastro and Hep 2011
Prevalence of NAFLD/NASH

<table>
<thead>
<tr>
<th></th>
<th>NAFLD</th>
<th>NASH</th>
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</thead>
<tbody>
<tr>
<td>General US adult population</td>
<td>25% (6-33%)</td>
<td>1.5-6.5%</td>
</tr>
<tr>
<td>Obesity</td>
<td>75%</td>
<td>19%</td>
</tr>
<tr>
<td>Severe Obesity</td>
<td>89%</td>
<td>36%</td>
</tr>
<tr>
<td>Type 2 diabetics</td>
<td>76%</td>
<td>25-30%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>50%</td>
<td></td>
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<tr>
<td>Pediatric population</td>
<td>All children: 9.6%</td>
<td>Obese children: 38%</td>
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Prevalence of Self-Reported Obesity Among U.S. Adults by State, 2012

Body Mass Index (BMI) of 30 or higher

Prevalence of Self-Reported Obesity Among U.S. Adults by State 2013

Body Mass Index (BMI) of 30 or higher
Prevalence of Self-Reported Obesity Among U.S. Adults by State 2014

Body Mass Index (BMI) of 30 or higher

NAFLD is common

US adult population 300 million

NAFLD 25%
NASH 1.5 - 6.5%
Cirrhosis 0.3 - 1%

Putting things in perspective:
Type 2 Diabetes 8%
HCV Infection 2%
HCV Cirrhosis 0.5%
Colorectal cancer 0.3%

1 to 3 million people may have NASH-cirrhosis

NASH is a Serious Condition

HCC incidence of 2.6% for NASH-related cirrhosis
NAFLD/NASH: Serious Condition

- NAFLD patients have a higher overall mortality, mostly related to cardiovascular disease
- NASH patients have increased liver-related mortality rate
- NASH has become the second indication for Liver Transplantation in the United States after Hepatitis C

Younossi Hepatology 2015, Wong Gastro 2015

NAFLD is a Silent Disease

Asymptomatic

Liver Enzymes Elevation/
Fatty Liver on imaging

Symptomatic

Hepatomegaly-Fatigue

Decompensated Cirrhosis

Evaluation of Suspected NAFLD

Rule out alternative causes of liver disease:
- History - Evaluation of co-morbidities
- Medications, Alcohol use quantification
- Physical Exam
- Imaging, Serological workup for: viral/autoimmune/genetic causes
- Consideration for liver biopsy versus noninvasive testing for diagnosis and staging

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NAFLD: Management Strategies

- Cirrhosis Mgmt
- Liver-directed Pharmacology
- Targeting components of metabolic syndrome
- Lifestyle Modification

No FDA-Approved Therapy for NASH is Available

- **Metformin**: Not a primary treatment for NASH
- **Pioglitazone**: Weight gain, bone loss, GI upset, fatigue, and lower extremity edema
- **Antioxidants (vitamin E)**: Long-term safety is questionable (increased all-cause mortality and risk of prostate cancer)
  - Not tested in diabetic patients
- **Lipid-lowering drugs**: Not a primary treatment of NASH
  - Not validated in clinical trials
- **Pentoxifylline**: Randomized controlled trials led to inconsistent results
- **UDCA**: Most randomized controlled trials did not show positive results

Weight Loss is the Cornerstone of NAFLD Treatment

- Fibrosis (45%)
- NASH Resolution (64-90%)
- Ballooning/Inflammation (41-100%)
- Steatosis (35-100%)
- Weight loss ≥ 10%
- Weight loss ≥ 7%
- Weight loss ≥ 5%
- Weight loss ≥ 3%
# Conclusion

- Increasingly prevalent
- “Silent” Disease
- Can be severe (NASH)
- So far there are no specific therapies
- Lifestyle modification (weight loss) is the key intervention

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# Q&A

**(10 Minutes)**

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The Liver

- Largest organ in the body (1.4 kg – 3 lbs)
- Located in the Right Upper Quadrant
- Right and left lobes, 8 segments
- Porta hepatis = Portal Vein, Hepatic Artery, Common Bile Duct

Liver Anatomy

Healthy

- Length 10-15 cm
- Span 15 cm
- Weight 1.5 kg

Cirrhotic
Stages of Liver Fibrosis (Scarring)

- Stage 1: Minimal fibrosis
- Stage 2: Mild fibrosis
- Stage 3: Moderate fibrosis
- Stage 4: Severe fibrosis

Staging the Severity of Liver Disease: Liver Biopsy

- Percutaneous liver biopsy
- Transjugular liver biopsy
Staging the Severity of Liver Disease: VCTE

Causes of Cirrhosis

INFECTIONOUS | BILIARY/ Autoimmune | TUMORS/Toxins | VASCULAR | METABOLIC
--- | --- | --- | --- | ---
Chronic viral hepatitis B, C, D | Primary biliary cirrhosis | Alcohol | Budd-Chiari, Veno-occlusive disease | Fatty liver
Schistosomiasis | Autoimmune hepatitis, Sarcoidosis | Vitamin A intoxication | Chronic congestive heart failure | Wilson's disease
Syphilis | Congenital biliary disorders | VOD | A1-anti-trypsin deficiency, other inherited metabolic diseases

Cirrhosis → Portal Hypertension
Complications of Cirrhosis

- Ascites
- Esophageal varices
- Encephalopathy
- HPS
- HRS
- HCC

Skin Manifestations of Cirrhosis

- Erythema nodosum
- Spider naevi
- Palmar erythema

Esophageal Varices
Management of Ascites

- Liver US at baseline and then every 6 months.
- Evaluate for HCC.
Natural History of Cirrhosis

- Compensated stage: progressing fibrosis
  - Usually no symptoms
  - 10-12 years
  - Liver cancer risk
  - Varices develop
  - Spleen enlarges
  - Platelets drop
  - INR increases

Natural History of Cirrhosis (cont.)

- Decompensated stage: worsening portal HTN: 5%/year
  - Ascites
  - Variceal bleed
  - Hepatic encephalopathy, lethargy confusion
  - Kidney injury: hepatorenal syndrome
  - Cancer of liver
  - Lung injury
  - Requires liver transplantation to survive

MELD Score

- MELD = (0.957 x LN(creatinine) + 0.378 x LN(bilirubin) + 1.12 x LN(INR) + 0.643) x 10
  Capped at 40

- Higher MELD: worse prognosis and increased mortality
Orthotopic Liver Transplantation

Q&A – Cirrhosis
(10 Minutes)

“Ask the Experts” Patient Education Program

Mousab Tabbaa, MD
ALF Medical Advisory Committee Chair
President, North Shore Gastroenterology and Endoscopy Centers
Wellness

Liver Wellness = Wellness

- **HEALTHY DIET:** What to eat?
  - Coffee?
  - Alcohol?
- **EXERCISE:** How much?
  - What type?
- **TOXINS:** Polypharmacy?
  - Over-the-counters?
  - Herbal supplements?
Increased BMI is Bad for You!

- Coronary artery disease
- Hypertension
- Increased cholesterol and triglycerides
- Diabetes
- Atherosclerosis
- Strokes
- Peripheral vascular disease
- Dementia
- Fatty liver and Cirrhosis
- Arthritis
- Impotence
- Cancer of various organs

Body-mass Index and Incidence of Cancer: A Systematic Review and Meta-analysis of Prospective Observational Studies

30% WORKOUT

70% DIET
Effect of Aerobic Exercise Training Dose on Liver Fat and Visceral Adiposity

- All exercise levels, irrespective of volume (minutes/week) or intensity, were effective in reducing liver and visceral fat by small but clinically important amount in obese adults.
- These changes were observed even without clinically significant weight loss.
- There was no difference between different exercise regimens for these benefits.
Exercise and Improvement of NAFLD: Practical Recommendations

- There is good quality evidence to support that regular exercise is beneficial in reducing the risk of NAFLD.
- Both aerobic and resistance training regimen are equally effective in reducing liver fat even in the absence of weight loss.
- There are no data to support that exercise alone without weight loss can improve or reverse NASH.
- Hence, lifestyle interventions utilizing both exercise and caloric restriction inducing weight loss (loosing approximately 5-10% of body weight) are needed.

editorial by Loomba R et al

Western Dietary Pattern and Fast Food

- Consumption of fructose, soft drinks, meat, saturated fat
- Consumption of fiber, PUFA, fish or omega-3 and vitamins

In one study > twice a week = 4.5 kg extra body weight = two fold greater insulin resistance
In other study: 18 healthy young students with at last 2 fast food meals a day for 4 weeks
11 had elevated ALT at one week

- In clinical evaluations of subjects with ALT
- Questions about alcohol and soft drink
- Recent excessive intake of fast food
Alcohol Consumption and the Risk of Cancer
A Meta-Analysis

Vincenzo Bagnardi, Ms.C., Marta Blangiardo, Ms.C., Carlo La Vecchia, M.D., and Giovanni Corrao, Ph.D.

- Alcohol consumption has been linked to an increased risk for various types of cancer.
- A combined analysis of more than 200 studies (i.e., a meta-analysis) found that alcohol most strongly increased the risks for cancers of the oral cavity, pharynx, esophagus, and larynx.
- Statistically significant increases in risk also existed for cancers of the stomach, colon, rectum, liver, female breast, and ovaries.
- Concurrent tobacco use, which is common among drinkers, enhances alcohol’s effects on the risk for cancers of the upper digestive and respiratory tract.
- The analysis did not identify a threshold level of alcohol consumption below which no increased risk for cancer was evident.
What do we recommend our patients with NAFLD about alcohol use?

• Heavy alcohol consumption has many harmful effects on liver and should be discouraged regardless whether an individual has NAFLD or not.
• Emerging epidemiological data suggest that light to moderate drinking may have favorable effects from a liver standpoint.
• But most studies are cross-sectional in nature and utilized surrogates such as aminotransferases and liver imaging.

What do we recommend our patients with NAFLD about alcohol use? (cont.)

• It is not clear if cardiovascular and metabolic benefits of light alcohol consumption observed in general population are extended to those with NAFLD.
• There are emerging studies to suggest that even light alcohol consumption may increase the risk of cancers (e.g., breast and colon).
• Until further data become available, we believe that individuals with NAFLD should avoid alcohol consumption of any type or amount.

Coffee
Coffee Consumption and Liver Function

- Drinking moderate amounts of coffee may help to reduce the risk of liver cancer.
- Moderate coffee consumption may also be related to a slower progression of liver disease (milder course of fibrosis).
- Seen in patients with alcoholic liver disease, non-alcoholic liver disease and Hepatitis C.
- Several different coffee components are being investigated. - Kahweol and cafestol, naturally-occurring compounds in coffee, are being studied for their anti-carcinogenic effects. - The anti-viral properties of chlorogenic and caffeic acids are also under investigation.

Drugs & Liver Injury

Fatal Combination
Thank You!!

Q&A – 10 Minutes

"Ask the Experts" Patient Education Program