You’ve Got To Move It, Move it!!!
Shaking the Fat Out of Fatty Liver Disease

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Speaker Introduction

• Debra Browne is a PNP in the division of gastroenterology at Children’s Hospital Los Angeles. She specializes in GI motility problems and also is a member of the fatty liver team. She was nominated for the CHLA Humanism Award, for providing outstanding compassionate care.

Disclosures -- None

Non-Alcoholic Fatty Liver Disease – NAFLD
Learning Objectives:
1. Describe the disease process for NAFLD
2. List comorbidities of NAFLD
3. Identify and interpret NADFLD screening guidelines/recommendations
4. Explain appropriate interventions to manage the disease
5. Review current research topics related to the NAFLD management

Here’s your LIVER

Interesting Liver Facts
--largest solid organ in the body—made up of 2 sections: Right and left lobes
--second largest organ in your body; skin #1
--located under right rib cage
--weighs about 3 pounds
--size of a football
Interesting Liver Facts—continued

• Holds 13% of body’s blood volume at any given time
• 3 pints of blood are filtered through the liver every minute
• Performs > 300 things at a time
• Only found in vertebrates

The Liver is a METABOLIC ORGAN

ENDOCRINE ORGAN
• Makes glucose
• Secretes proteins
• Site of fatty acid oxidation and ketogenesis
• Synthesizes of coagulation factors
• Regulates hormones (insulin and estrogen), stores glycogen, gluconeogenesis

The Liver is a METABOLIC ORGAN

EXOCRINE ORGAN
• Bile acid synthesis
• Main site of cholesterol and phospholipid metabolism

IMMUNE ORGAN
• Defends body against enteric bacteria and bacterial toxins, fight autoimmune disorders

Fatty Liver Disease Facts

• Most common liver disease in the US
• Effects 20 million people
• 8.6 million have the severe form called NASH (non-alcoholic steatotic hepatitis)
• #3 indication for liver transplantation in adults

More Fatty Liver Disease Facts

• Effects 10% of children in US, M > F
• 1% are 2 - 4 years old
• 15 - 17% are 15 - 19 years old
• From 1988-2010 NAFLD has increased and is now the most common liver disease in children (1)

More Fatty Liver Disease Facts

• Hispanic and Native American Populations have greatest incidence
  — genetic polymorphism PNPLA3
• Maternal Gestational Diabetes may increase the risk due to: fetal hyperinsulinemia increases adiposity, macrosomia and possibly decreased leptin sensitivity

(1) American Liver Foundation, Pediatric NAFLD, 6/14/10.
**WHY are kids getting so fat??**

- Role of food in Society/Culture/Family
- Visual appearance of obesity
- Role of extended family as caretakers
- Access to fresh fruits/veggies
- Cost of fresh fruits/veggies
- Increasing Obesity related to sugar additives in purchased and processed foods

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**OBESITY**

- Defined by BMI percentile
  - Normal = 5 to 84.9 percentile
  - Overweight = 85 to 94.99 percentile
  - Obese > 95 percentile
  - Morbid Obesity = > 99 percentile = 4-5% of US Youth
- Of about 2.7 million U.S. children could be considered **morbidly obese**. ... "With 1.3 percent of teens at or above a BMI of 40, that translates into 418,000 teens" *(1)*

*(1) https://www.mayoclinic.org/symptoms-causes/syc-20354827

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**2019 RWJ Obesity Study**

- Rates were unchanged 2016-2019.
- Of 4.8 million kids aged 10-17, about 15% were obese in 2017-2018.

**Ethnic Disparities:**
- Black 22%
- Hispanic 19%
- Whites 12%
- Asian 7%

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**2019 RWJ Obesity Study —Risk increases when . . .**

- 22% higher risk of obesity when HHI falls below poverty level
- Only 9% risk when HHI = 4x poverty level

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**2019 RWJ Obesity Study**

**HIGHEST** rates of obesity
- Mississippi 25.4%
- W. Virginia 20.9%
- Kentucky 20.8%
- Louisiana 20.8%
- Michigan 18.9%

- Robert Wood Johnson Foundation news release 10/10/2019
2019 RWJ Obesity Study

- LOWEST rates of obesity
  - Utah 8.7%
  - Minnesota 9.4%
  - Alaska 9.9%
  - Colorado 10.7%
  - Montana 10.8%

- Robert Wood Johnson Foundation news release 10/10/2019

Obesity

- Obesity has tripled in the last 4 decades
- Prevalence of Obesity increases with age
  - Young childhood = 14%
  - School age = 18.4%
  - Adolescence = 20.6%
  - Adulthood = 39.8%

- Hales, Carroll, Fryar & Ogden, 2017
- www.cdc.gov/obesity/childhood/prevalence.html

HISTORY - comorbidities

- Obstructive Sleep Apnea (OSA)
  - hard to breath and exercise
  - get tired fast
  - poor school performance –fall asleep in class
- Hypertension
- Type 2 Diabetes
  - > 5,000 new case each year in kids under 20 years old
  - Greater morbidity than adults with Type 2 Diabetes

Comorbidities -- continued

- Insulin Resistance = Impaired insulin signaling interfering with glucose transport
  - metabolic syndrome(hyperglycemia and dyslipidemia)
  - decreased insulin clearance
- Lab tests that suggest Insulin Resistance
  - HgbA1C > 6.5
  - Fasting Glucose >126 mg/dl
  - 2 hour Glucose TT >200

Comorbidities -- continued

- Heart disease—increased cholesterol and triglycerides
- Joint/Mobility problems i.e. SCFE
- Early onset puberty
- PCOS: hyperandrogenism, menstrual dysfunction, insulin resistance
NAFLD — Process

- Develops slowly over time
- Starts when fat builds up inside the liver
- Over time too much fat stays in the liver

NAFLD — Process continued

1. Normal
   - Flexible, normal size, normal fat

2. Fatty Liver (NAFLD)
   - Increased liver size with pockets of fat
   - Early inflammation

3. Steato-hepatitis (NASH)
   - Increased fat storage + inflammation
   - increased liver stiffness
   - Bridging/ballooning hepatocytes
   - Beginning of cell damage

4. Cirrhosis — fat + inflammation + stiff + scaring,
   - weakness
   - abdominal pain
   - swelling hands/feet/abdomen
   - bruising, bleeding

5. Liver failure and need for transplant
Screening Recommendations

• 2007 AAP
  - Biannual screen AST/ALT starting at 10 yr old
  - BMI > 95 %-tile
  - BMI > 85-94 %-tile if there are cardiac or metabolic risk factors
• 2008 Endocrine Society
  – BMI > 85 %-tile with ALT

Program Referral Criteria

• AGE > 9 yrs. Old, now trending downward
• BMI > 85 %-tile
• ALT > 45
• +/- Abdominal Ultrasound enlarged echogenic liver consistent with fatty infiltration

NAFLD Diagnostic Screening

BASELINE SCREENING

- CBC
- CHEM 14
- AST—need to be lower than ALT or probably NOT fatty liver
- ALT—increases with hepatocellular injury
- GGT—increases with biliary obstruction
- HgbA1C
- Lipid panel

ULTRASOUND YES/NO?????

- Pros: Non-invasive
- Cons
  - Low sensitivity/specificity particularly lower degrees of steatosis
  - Not recommended for screening in NASPGHAN Guidelines
  - Cannot differentiate between NASH, NAFL

Lab Limitations

Limitations of ALT

- Poor correlation with histology
  - Some studies suggest AST, GGT better correlated with fibrosis
  - ALT changes even with placebo!
- Fluctuations over time
- Cannot always differentiate between NAFL and NASH
**NAFLD Diagnostic Secondary Screening**

**Infectious Causes**
- Hep A=HAV Ig G/IgM
- HBSAG, HBSAB
- HCV Ab

**Celiac Diagnostic**
- TSH/Free T4
- Serum Iron, TIBC, Ferritin

**NAFLD Diagnostic Screening**

**Auto Immune Hepatitis**
- Total IgG
- SMA - Smooth Muscle Antibody—looks at auto immune hepatitis vs other liver injury
- LKM - Liver Kidney Microsomal Antibody—increases in autoimmune hepatitis
- ANA—increases in autoimmune diseases

**Additional Screening**
- A1AT level—low or absent in liver disease
- Lysosomal Acid Lipase Deficiency
- Soluble Liver Antigen

**Non-invasive study**

- Magnetic Resonance Elastography
  - Higher study completion success rate (94 to 84%)

*Images courtesy of Drs. Daniel Prokhorov and Swaj Bimal, Dept of Radiology, GOSH*

**To Biopsy or Not to Biopsy?**

**PROS**
- Can distinguish between NAFLD and NASH
- Clinical prognosis depends on histology
- NASH 25-30% risk of progression
- Early onset pediatric fibrosis more aggressive?
- Rule out other liver diseases (AIH, Wilson)
- Initiate more aggressive Rx

**CONS**
- Risk 1:10,000 risk of death (in adults)
- Sampling error
- Expense
TREATMENT—SMART GOALS

Specific
Measureable
Attainable
Realistic
Timely

Treatment

• #1 stop all beverages with sugar
• Decrease restaurant /fast food meals
• Decrease portion sizes
• Decrease frequent snacking
• Decrease skipped meals.
• Continue to offer SNAP assistance to qualifying families.
  • 1/3 of kids 4 yrs old and younger participate in SNAP each month

Treatment

• PREVENTION
• EDUCATION
• Go outside and play!!!
• Weight loss (10 % body weight)
• “Solamente Agua!”
• Vitamin E 400 units BID in biopsy proven NASH x 2 years
• Gastric sleeve—1600 procedures per year (replaced the more complicated RYGB)
• Liver Biopsy every 2 years to monitor disease

Research

• HEROES—USC
• SuperHEROES-CHLA
• UCSD—teen boys,
  • diet = 3% sugar
  --8 week trial:
  --steatosis decreased by 25%
  down to 17%.

FibroScan

Treatment Barriers

• It’s just not safe to play outside
• Healthy food is expensive and harder to find
• Transportation limitations
• Caretakers sabotage the efforts
• Limited kitchen access in multi-family or single room living arrangements
• Homelessness, e.g. living in car, food insecurity
What I have learned

• The problem is ASYMPTOMATIC “I feel great/fine, nothing hurts” therefore it is hard to make changes
• Liver enzymes results do NOT correlate with biopsy results
• A LIVER BIOPSY is the “Gold Standard” and is currently the only reliable method to stage fibrosis
• MRI Elastography is not an accurate way to predict biopsy results
• FibroScan may be helpful as a monitoring tool
• Provider and family frustration with poor compliance with recommendations for weight loss

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