Non-Alcoholic Fatty Liver Disease

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Disclosures

- Research
  - Gilead –NASH trial
  - Intercept – NASH trial
- Advisory Board
  - Pfizer – IBD
  - Lupin – Encephalopathy
  - Intercept – PBC
- Speaker Fees
  - Gilead - post-conference update
- I will not be recommending the current or investigational drugs of these companies

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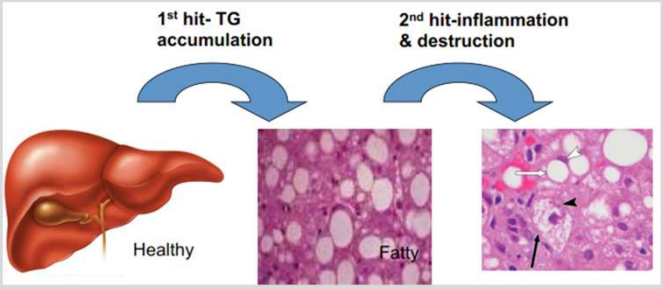
Terminology

- Fatty liver disease = replacement by fat of the cytoplasm of hepatocytes with displacement of the nucleus (a.k.a. macrovesicular steatosis)
- Steatohepatitis = steatosis with evidence of inflammation or liver damage such as:
  - Evidence of significant liver fibrosis
  - Histology showing lobular or portal inflammation
  - Histology showing cell necrosis: Mallory bodies and balloon degeneration



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NAFLD

- Non-Alcoholic Fatty Liver Disease (NAFLD) = macrovesicular steatosis not caused by significant alcohol intake
- Significant alcohol intake
  - Men >40g/day (3 beers)
  - Women >20g/day (1.5beers)
  - Standard serving = 14g
- Causes of NAFLD
  - **Obesity and metabolic syndrome**
  - Hypertriglyceridemia
  - PCOS
  - Rapid weight loss
  - Medications
  - TPN
  - Celiac disease
  - Wilson's disease
  - Hepatitis C
  - Several genetic metabolic syndromes
- Possible confusion
  - Iron overload and steatosis look the same on US
  - Fatty liver and alcohol increase Ferritin and transferrin saturation

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Incidence

- NAFLD
  - 69-100% of obese patients
  - 34-95% of diabetics
  - 20%-80% of patient with hypertriglyceridemia
  - 10-15% in non-obese
- NASH
  - 15-20% if BMI >35
  - 2-3% if BMI <35
  - 67% if DM with NAFLD
- Cirrhosis
  - 3-5% in obese
  - <1% in non-obese
  - DM triples risk of progression to cirrhosis from any cause of liver disease
  - 1/3 of patients with cirrhosis have diabetes

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What will kill these patients?

- Leading causes of death in NAFLD
  - Cancer 28%
  - Heart Disease 25%
  - Liver Disease 13%
- Most patient with NAFLD won't have complications of chronic liver disease. How do we identify those that might?

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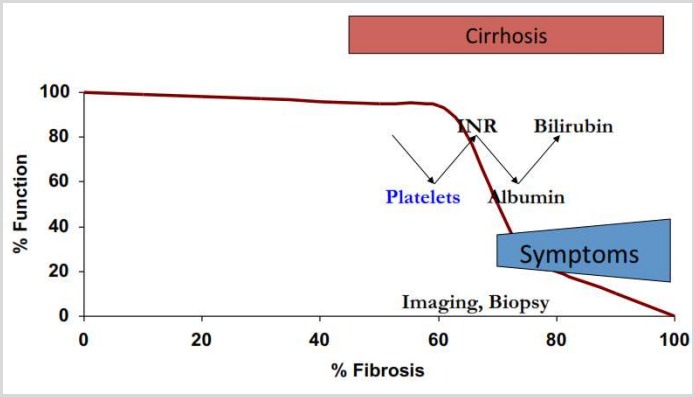
Cannot rely on symptoms or liver function tests alone



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Who needs further assessment:

Liver enzymes elevated:

- Need assessment of fibrosis and need to rule out other causes of elevated liver enzymes

Liver enzymes are not elevated do non-invasive testing of fibrosis if:

- Diabetic
- Obese
- Uncontrolled severe hypertriglyceredemia
- Will be starting hepatoxic medications

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What non-invasive test of fibrosis are available in Victoria?

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Serum Tests

- APRI: uses AST and platelets , good at ruling in (spec >90%), not enough to rule out (sens ~70%)
- FIB-4: uses age, AST, ALT, platelets. Accuracy ~85%, best for ages 35-65
- http://www.hepatitisc.uw.edu/page/clinical-calculators/apri
  - In centers where elastography not available, FIB-4 is emerging as the first line screening test, to determine who should be referred to another center to have elastography
  - Edmonton uses 1.3 as cutoff to pre-screen populations from Northern Alberta and NWT
  - 85% of patients with FIB-4 < 1.3 will have elastography of <8 kPa, i.e. no significant fibrosis
- If using non-invasive testing, guidelines recommend combining serologic makers and elastography when both available

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Elastography

Change in velocity of a pulse of sound estimates liver stiffness in kPa

Two version available

- Realtime shear wave elastography, done as part of doppler US in Island Health radiology department
  - No cost to patient, but ~6 month wait
  - Order in VIHA US req ask for "shearwave elastography to assess fibrosis in patient with suspected NASH"
  - For advanced fibrosis (>F3) sens 89%, specificity 88%
- Fibroscan
  - Not publicly funded, available at Percuro at cost of $75 to patient, but can obtain quickly
  - Pulse elastography: Doesn't visualize whole liver, just takes a stiffness measurement
  - For advanced fibrosis (>F3) sens 91%, specificity 75%

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Liver Biopsy

- Offered in cases of diagnostic uncertainty, or discrepancy between non-invasive modalities
- Also offered to "confirm" advanced fibrosis and rule out competing etiologies in patient in whom non-invasive markers predict advanced fibrosis
- An imperfect gold standard
  - Biopsy taken from two areas of the liver yield different stage of Fibrosis 15-30% of the time
  - 1:10,000 risk of death
  - 25% have pain in the first 48h post biopsy
  - Risk of bleeding, pneumothorax, bile leak

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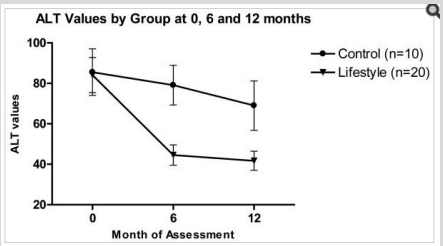
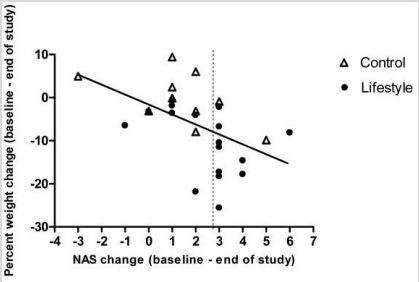
Treatment: Diet and Exercise

- Goal 10% reduction in body weight in 1 year
  - 3-5% reduction will improve steatosis
  - 7-10% reduction will improve inflammation
- No more than 1-2lbs per week





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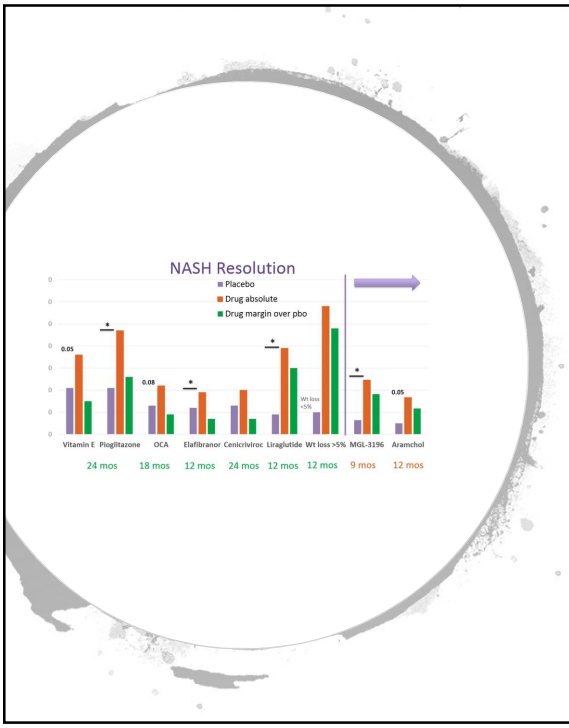

Many Treatment In The Horizon

- So far, no treatment is better than weight loss through diet and exercise
- OCA first positive Phase III interim analysis, based on regression of fibrosis, rather than NASH resolution
- Will likely take combination of drugs. ATLAS trial presently looking at this
- GLP-1 analogues shown most benefit, and already available and licensed to treat the two biggest risk factors of NASH : DM and Obesity

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Refer to Multidisciplinary Clinic

NAFLD is best treated as part of metabolic syndrome as a whole. Two clinics in the city specialize in this:

The Cardio-Metabolic Collaborative Clinic

- Consults in all aspects of metabolic syndrome
- Includes 12-week lifestyle program to help with weight loss
- Experienced in pharmacotherapy to aid in weight loss
- Ambulatory BP monitoring, stress testing, holter monitoring, OSA testing
- Individual and group counselling by dietician
- Fax 250-412-6464

Revive Lifestyle Clinic

- Near Westshore Centre
- Focus on nutrition, exercise, mindfulness for treatment of lifestyle associated illnesses
- Also provides general internal medicine consults, cardiac treadmill testing, ECG, and Holter monitoring
- Fax 1-866-573-8483

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Who needs GI follow up

GI needs to follow patients with cirrhosis to monitor for and treat liver related complications

Also consider referral to GI if:

- Diagnostic uncertainty
- Will start medication that may have hepatotoxicity
- Persistently elevated liver enzymes despite weight loss and treating metabolic syndrome

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