

The Unbearable Weight of Fatty Livers:

an overview of NAFLD diagnosis and treatment

or:

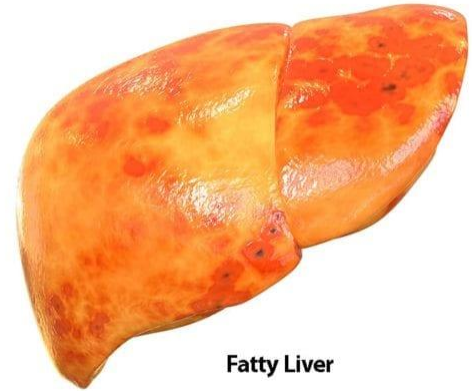
How to not get yelled at by Dr. Beaven and still take good
care of your patients

Drew MacQuarrie, MD

AST 76 / ALT 82

:L6

P₀:



Fatty Liver



SLEEPY INTERN

:L4

REST:

30 / 30

A FATTY LIVER APPEARED!

AST 76 / ALT 82

:L6

P₀:



Fatty Liver

SLEEPY INTERN

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Lifestyle Changes

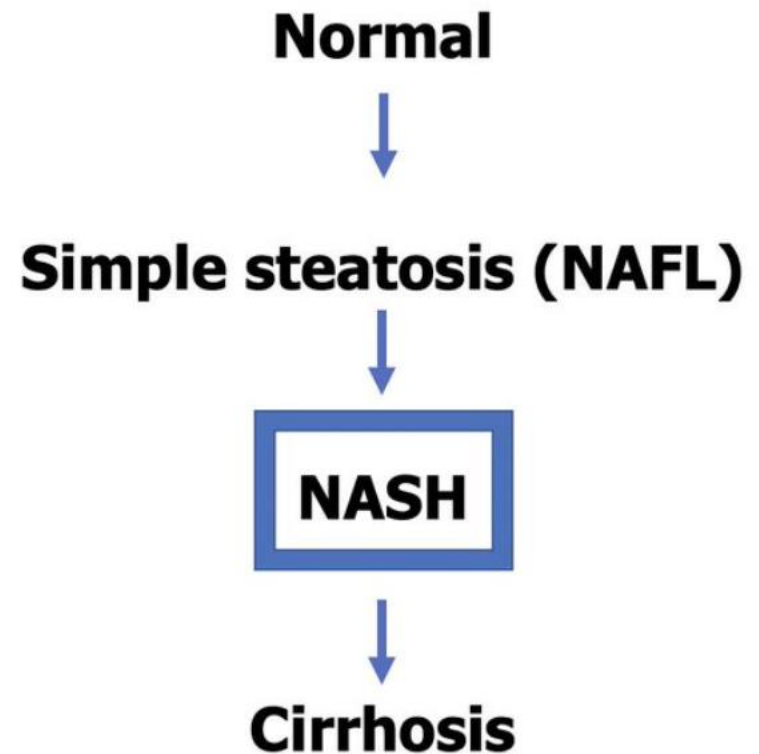
US q6m for 5-10 years

eConsult Beaven

RUN

NAFLD/MAFLD Terminology

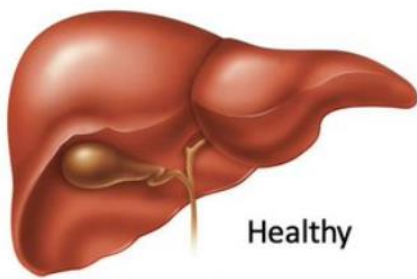
- **NAFL:** Hepatic steatosis w/o inflammation
- **NASH:** Hepatic steatosis **WITH** inflammation



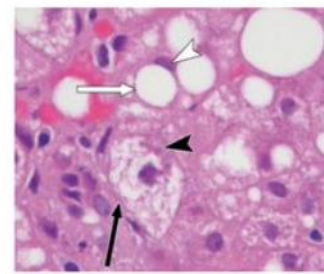
Pathogenesis

IR, TG accumulation, ER stress, Mito dysfunction

Adipose dysfunction, Dysbiosis, Inflammation



Steatosis
-just fat
-no injury

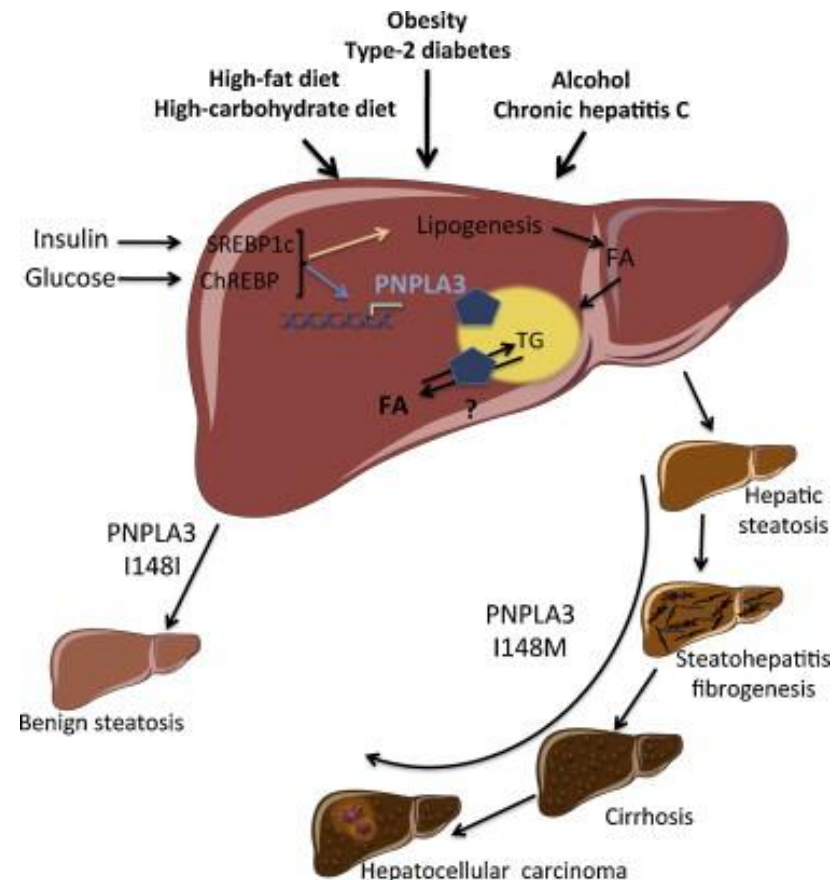


Steatohepatitis
-fat with
inflammation and
injury

- Occurs in a genetically predisposed patient (PNPLA3 etc)
- Usually with dietary and lifestyle issues leading to weight gain

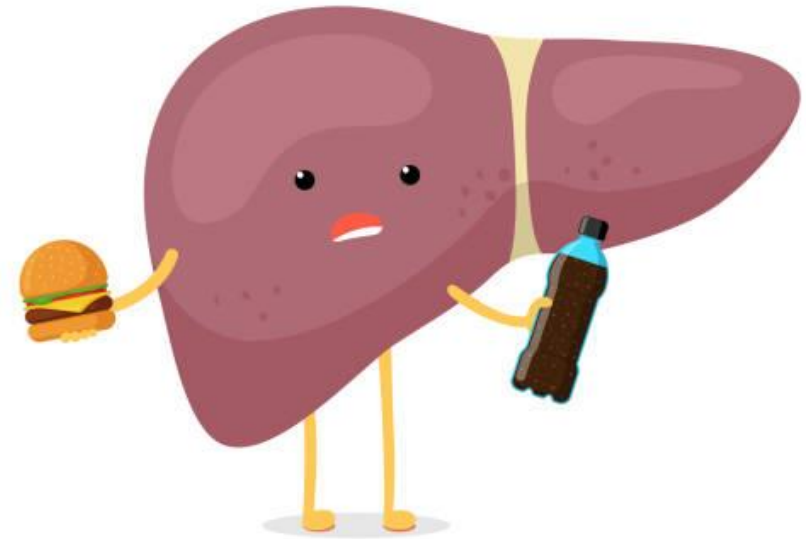
PNPLA3

- Patatin-like phospholipase (“Adiponutrin”)
- Mutation = ↑ risk
Alcoholic + Non-Alcoholic
Liver Disease
- Not clinically relevant
(currently)



Why it Matters?

- Most common chronic liver disease globally
- Risk factor for HCC
- #2 reason for Liver Tx in the US



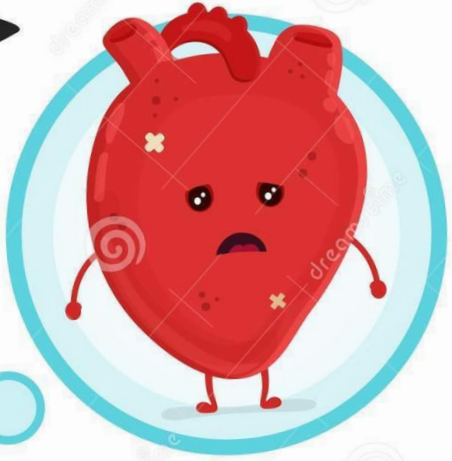
Epidemiology

- Increasing prevalence:
 - 1988-1994: 5.5%
 - 1999-2004: 9.8%
 - 2005-2008: 11%
 - Today?
 - Gen Pop: 20-25%
 - By US in 1^o care: 20-30%
 - DM Clinics: 60-100%
- Age 40s-50s
- M \approx F
- Hispanic Americans
- Risk Factors:
 - Diabetes
 - Central Obesity
 - Dyslipidemia
 - Metabolic Syndrome
 - Cholecystectomy?

TRICK QUESTION

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A TRICK

LESS TRICKY QUESTION

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P₀:



...an ibex?



A LESS TRICKY

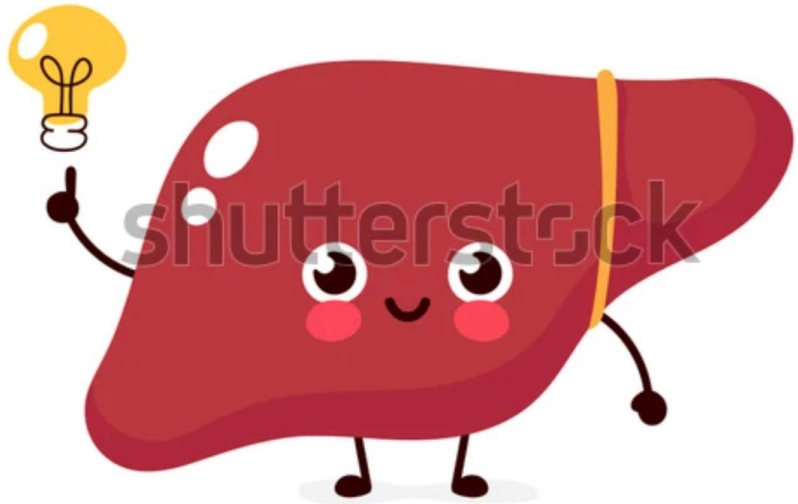
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Clinical Manifestations

- **Radiology**
 - US: ↑ echogenicity
 - CT: ↓ attenuation
 - MRI: ↑ fat signal



Diagnosis of NAFLD



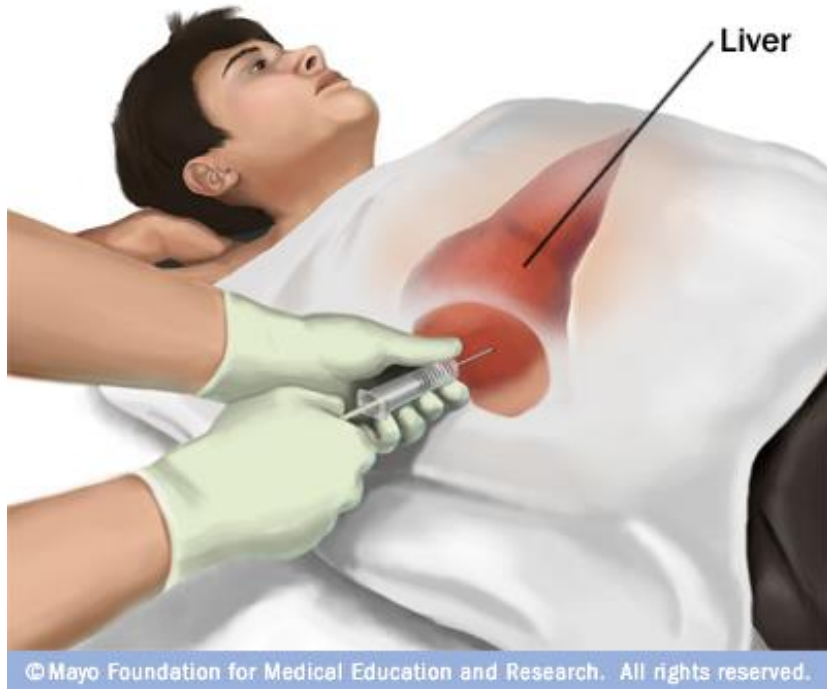
- Imaging
 - US
 - Qualitative
 - US-based Elastography
 - Quantitative
 - MRI-PDFF
 - Quantitative

And then there's biopsy...



- Liver biopsy is the only way to differentiate NAFL from NASH!
- So who do we biopsy?

Who gets a biopsy?



- Stigmata of cirrhosis
- Splenomegaly
- Cytopenias
- Ferritin $> 1.5x$ ULN
- **> 45 yo w/ Obesity or DM**

NAFLD Fibrosis

FACTS & FIGURES

NAFLD

< -1.45

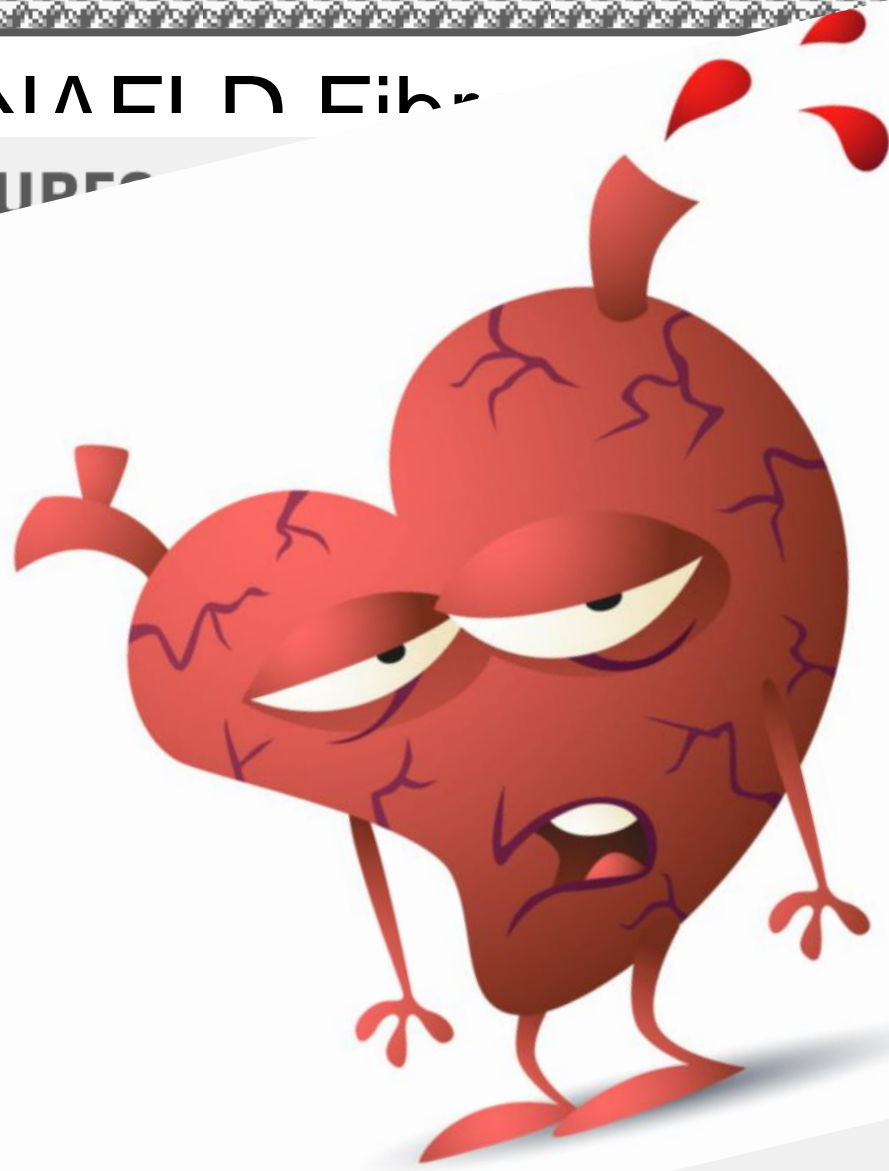
-1.455 -

> 0.675

Fibrosis Severity

- F0 = no fibrosis
- F1 = mild fibrosis
- F2 = moderate fibrosis
- F3 = severe fibrosis
- F4 = cirrhosis

erity



DHS Expected Practices



Health Services
LOS ANGELES COUNTY

- **eConsult?**

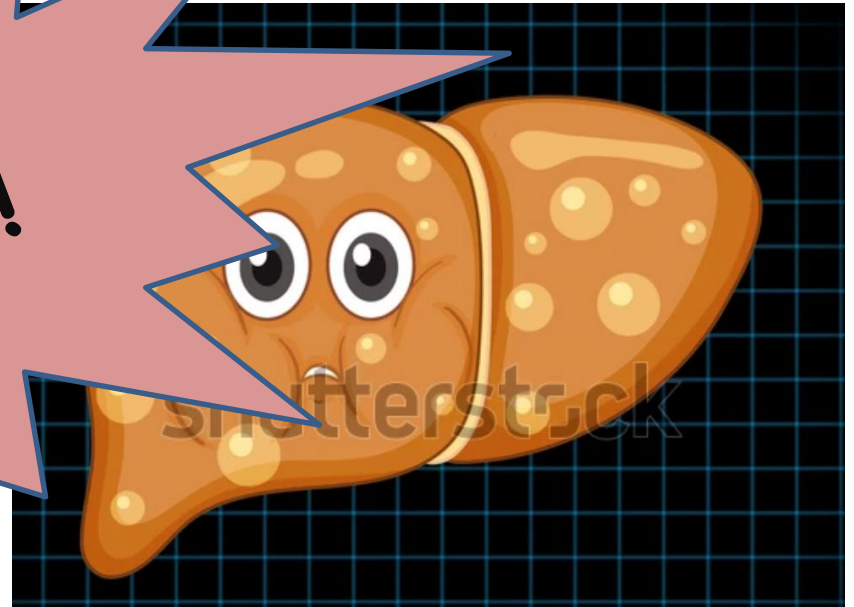
- Alk Phos > 3x ULN
- ALT > 5x ULN
- Total Bili > 2
- AST/ALT > 2 (w/o etoh!)
- Thrombocytopenia
- Rule-out labs positive

Management of NAFLD

- General Principles

- ↓

**STATINS
ARE OKAY!!!**



- FAs don't normalize, lose more!

Medications

- NASH w/o DM
 - Vitamin E 800 IU QD
 - Anti-Oxidant
 - Bleeding?
 - Prostate cancer?
 - Pioglitazone
 - Controversial w/o DM
 - Wt gain, CHF, Fracture



ANOTHER TRICK QUESTION

:L6

P₀:

WHAT DOES \$TNABTESVN
THIS MEAN TEXT?

30 / 30

ANOTHER ... APPEARED!

Medications

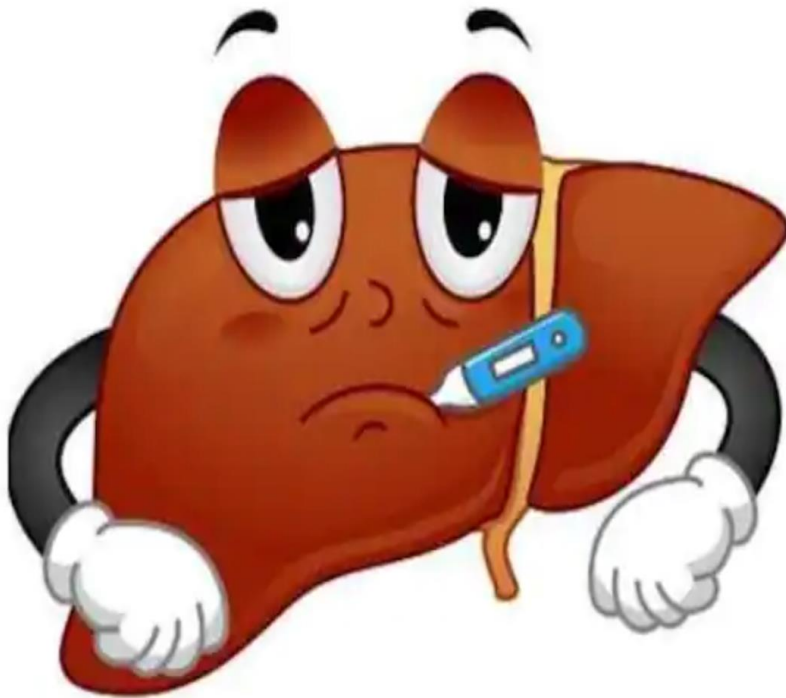
DHS Expected Practice?

- Furosemide > 0.12
- Prescription of vitamin E or thioglitzones (i.e. piaglitzone) is not recommended
- Vaccinate against Hepatitis A and B if not previously exposed or vaccinated
- Fatty Acids?
 - Aspirin?
 - FXR Agonists!



How are we Monitoring

And how often do we order that Ultrasound?



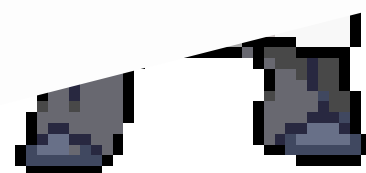
- LFTs q3-6 months
- Imaging?
 - Really only with change in clinical status
 - More wt gain
 - New DM, HLD, HTN
 - q3-4 years

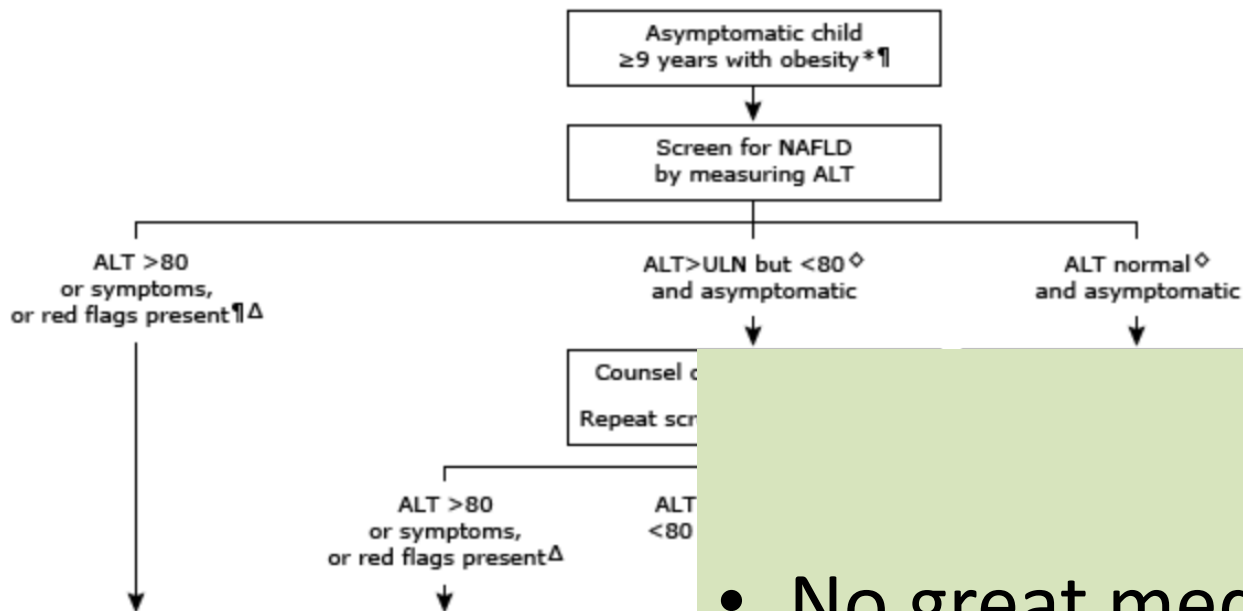
When to refer?

- LFTs \uparrow despite wt loss
- LFTs > 10

When to submit an eConsult to Hepatology:

- Laboratory findings atypical for uncomplicated NAFL:
 - Alkaline phosphatase > 3 ULN
 - ALT > 5 times the ULN
 - Total Bilirubin > 2
 - AST/ALT ratio > 2 in the absence of alcohol use
 - Low platelets
- Concern of findings suggesting Autoimmune Hepatitis, Wilson's Disease, Hemochromatosis or NASH related cirrhosis





Refer for a full evaluation, usually consisting of:

Screening labs:

- CBC with differential
- AST, GGTP, alkaline phosphatase
- Total and direct bilirubin
- Albumin, total protein
- Hemoglobin A1C
- Fasting lipid panel

Laboratory evaluation for other specific causes of liver disease:

- Infection (HAV, HBV, HCV, other chronic viral infections indicated by history)
- Celiac disease
- Hypothyroidism
- Autoimmune liver disease
- Genetic liver diseases (Wilson disease, hypobetalipoproteinemia, and alpha 1 antitrypsin deficiency, lysosomal acid lipase)

Consider liver biopsy ‡

- To assess for steatosis, inflammation/steatohepatitis, and fibrosis with copper measurement if Wilson disease is suspected

Imaging †

- Abdominal ultrasound to rule out anatomical abnormalities and assess for portal hypertension
- Possibly MRI-PDFF to measure liver fat

- No great medications
 - Vitamin E 400 IU BID
 - ⊘ Metformin
 - ⊘ Fish Oil

TAKEAWAYS

- NAFLD is not just a copy/paste problem
- Not all NAFL → NASH
- Weight loss is **CRITICAL**
- Consider medications
- Monitoring is important, but doesn't mean you need an US q12m



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Resources

- Browning, Jeffrey D., et al. “Prevalence of Hepatic Steatosis in an Urban Population in the United States: Impact of Ethnicity.” *Hepatology*, vol. 40, no. 6, 2004, pp. 1387–1395., <https://doi.org/10.1002/hep.20466>.
- “The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance from the American Association for the Study of Liver Diseases.” *Clinical Liver Disease*, vol. 11, no. 4, 2018, pp. 81–81., <https://doi.org/10.1002/cld.722>.
- Lazo, Mariana, et al. “Interaction between Alcohol Consumption and PNPLA3 Variant in the Prevalence of Hepatic Steatosis in the US Population.” *Clinical Gastroenterology and Hepatology*, vol. 19, no. 12, 2021, <https://doi.org/10.1016/j.cgh.2020.08.054>.
- *NAFLD for Primary Care*, <https://threadreaderapp.com/thread/1131608296501198850.html>.
- Romeo, Stefano, et al. “Genetic Variation in PNPLA3 Confers Susceptibility to Nonalcoholic Fatty Liver Disease.” *Nature Genetics*, vol. 40, no. 12, 2008, pp. 1461–1465., <https://doi.org/10.1038/ng.257>.
- Ruhl, Constance E, and James E Everhart. “Relationship of Non-Alcoholic Fatty Liver Disease with Cholecystectomy in the US Population.” *American Journal of Gastroenterology*, vol. 108, no. 6, 2013, pp. 952–958., <https://doi.org/10.1038/ajg.2013.70>.
- Starekova, Jitka, et al. “Quantification of Liver Fat Content with CT and MRI: State of the Art.” *Radiology*, vol. 301, no. 2, 2021, pp. 250–262., <https://doi.org/10.1148/radiol.2021204288>.

Questions?!?

