The Fatty Inflamed Liver  
by Dr. Mona Morstein

The obesity epidemic in the US today, whereby 70% of the population is now overweight, obese, or grossly obese, has dangerous implications for hepatic health in our country. The most commonly diagnosed liver disease in the US is nonalcoholic fatty liver disease (NAFLD), which can progress to nonalcoholic steatohepatitis (NASH). NAFLD also is the main reason that patients have elevated hepatic function tests in the US.

Pathophysiology

The liver typically contains about 5% fat, and when the amount increases to 10%, or the liver is defined as having steatosis, this is a fatty liver. If this is not due to alcohol intake, it is termed NAFLD. When patients have abdominal fat, there is a regular flow of free fatty acids to the liver. This innately is a benign condition that causes macrovesicular fat accumulation in the liver, whereby fat in the hepatocyte, the liver cell, displaces the nucleus to the edge of the cell and risks causing the hepatocyte to burst.

In stage 2 of this condition, when it advances, the patient develops NASH. The inflammation develops due to lack of antioxidants and "ballooning degeneration" (BD). BD occurs when the swollen hepatocytes burst, which attracts lymphocytes and other inflammatory cells that release cytokines, TNF-alpha, interleukins, hydrogen peroxides, and superoxides, causing hepatocellular damage, which over the years can destroy the liver. In fact, the three main reasons that the liver develops scarring, fibrosis, cirrhosis, and failure, requiring liver transplantation, are alcohol use, chronic hepatitis C, and NASH.²

NAFLD Statistics

Approximately 30% of the US population in all ages has NAFLD; 3% has progressed to NASH. It is seen most in Caucasian and Hispanic patients, but occurs in all races. It’s closely connected to metabolic syndrome. In fact, more than 90% of NAFLD patients have at least one of these problems: obesity, insulin resistance, impaired fasting glucose, elevated triglycerides, elevated LDL cholesterol, hypertension. 33% of NAFLD patients have at least three of those features associated with metabolic syndrome. In the reverse view, patients with metabolic syndrome have a 3 times greater risk of developing NASH and fibrosis. NAFLD is seen in 70% of type 2 diabetic patients, and up to 20% of these patients with NAFLD/NASH develop cirrhosis. Last, specifically regarding obese patients, 70% to 80% of obese patients and up to 100% of morbidly obese patients have NAFLD.³

NAFLD Etiology

The main etiological risk factor for developing NAFLD is insulin resistance, especially in the overweight or obese patient.⁴

There are many causes of NAFLD outside obesity and insulin resistance. The other risk factors for developing NAFLD include:

• fulminant or chronic hepatitis, usually C;
• drugs used for more than six months: valproic acid, corticosteroids, tamoxifen, estrogens, methotrexate;
• environmental factors: organic solvents, PCBs, petrochemicals, dimethylformamide;
• metabolic abnormalities: galactosemia, glycogen storage disease, homocystinuria, Wilson's disease, hemochromatosis;
• nutritional status: overnutrition, starvation diet, total parenteral nutrition, protein energy malnutrition, celiac disease/malabsorption syndromes, vitamin A toxicity;
• surgery: bariatric surgery causing rapid weight loss;
• conditions: alpha-1 antitrypsin deficiency, hyper- or hypothyroidism, primary biliary cirrhosis, primary sclerosing cholangitis.⁵

NAFLD/NASH Signs and Symptoms

In the majority of patients, patients present asymptomatically, and it’s the initial labs that uncover the NAFLD. Some patients can feel fatigue or malaise, but identifying that as solely from NAFLD is difficult, as patients present with obesity, poor diet intake, lack of exercise, and other factors that in themselves could cause poor energy and stamina.⁶

Signs of NAFLD/NASH may include: BMI >30; insulin resistance signs such as acanthosis nigricans, skin tags, waist measurement,
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- hypertension, high triglycerides; abdominal fat; hepatomegaly; splenomegaly; signs of cirrhosis such as spider angiomas, esophageal varices, gynecomastia, ascites, jaundice.

Diagnosis

Of course, basic blood work would likely pick up insulin resistance and metabolic syndrome, as mentioned above. However, there are lab values much more specific to NAFLD/NASH.

Usually the very first lab result elevated indicating that NAFLD has developed is serum ferritin. Serum ferritin is elevated for three main reasons — hemochromatosis, bacterial infection, or as an acute inflammatory marker. In its latter role it is elevated with fatty liver. A physician should always include ferritin in a basic blood work panel, and if it is elevated in a patient, rule out severe bacterial infection by patient presentation, and rule out hemochromatosis via an iron panel. If the percent saturation is normal, that genetic condition is ruled out. The next step would be to do an abdominal ultrasound.

Other lab values that may be elevated include GGT, although in my experience, ferritin is elevated much more often than GGT. If NASH is developing, then one might see ALT (alanine aminotransferase) and AST (aspartate aminotransferase) elevation; but for NASH, ALT > AST. Elevated aminotransferase enzymes do not correlate with intensity of NASH. In those cases, one would also have to rule out chronic viral or autoimmune hepatitis conditions (or other etiological factors), as well as alcoholism.

Some labs also do blood work to help discern if the liver has developed fibrosis, as otherwise occasionally a patient must undergo a liver biopsy. These tests, such as FibroSpect II from Prometheus Labs or FibroSure from LabCorp, measure various biomarkers that are used to help interpret if there is no/mild or severe fibrosis; they are both poor in the middle-ground interpretation, if there is moderate scarring.

The abdominal ultrasound discerns fatty liver when at least 15% fatty content exists, but it cannot differentiate NAFLD from NASH. The lab report will read positive echogenic areas consistent with fatty liver. Neither a CT scan nor MRI is helpful in further diagnosis. If further understanding of liver tissue is required, to know the cellular health of the hepatocytes, the gold standard is a liver biopsy, which then grades (macrovesicular steatosis 0–3; necroinflammatory activity 1–3) and stages (fibrosis 1–3; cirrhosis) the liver tissue.

NAFLD/NASH Prognosis

When a patient has NAFLD, 30% will progress to NASH, 30% will remain stable, and 30% will improve without pharmacologic intervention. NAFLD is reversible if the liver is not yet cirrhotic. An article in Hepatology Journal proved that patients who lost 5% or more of their body weight over nine months had improvement in insulin resistance and loss of fatty liver. The Southern Medical Journal had a study showing that reversal of fatty liver was seen based on exercise, weight loss, and the complete avoidance of alcohol.

Treatments for NAFLD/NASH

Standard Allopathic Care

There is not standard treatment specific for NAFLD/NASH. Alcohol is avoided, weight loss is advocated, exercise is recommended, and bariatric surgery is considered for particularly grossly obese patients.

The most important aspect of controlling fatty liver and reversing it is weight loss. However, weight loss must occur slowly — rapid weight loss or starvation diets or bariatric surgery can worsen NASH and lead to cirrhosis and liver failure. Rapid weight loss is defined as > 3.5 lb (1.6 kg) a week, with the ideal weight loss for effectiveness and hepatic safety being 1 to 2 lb/week. In this way, the liver is not flooded with a massive release of free fatty acids and their inflammatory irritation.

MDs have used various pharmaceuticals, such as thiazolidinediones, but those are pretty much off the market due to established side effects of their usage. Other drugs, such as Glucophag (metformin), Byetta (exenatide), statins, antiobesity drugs, and ursodeoxycholic acid, have been tried with various degrees of success.

Bariatric surgery has included both gastric banding, which regressed NASH, and the more extreme Roux-en-Y, which reversed fatty liver in 89% to 100% of patients but caused dumping syndrome, stomach staple failure, nutritional deficiencies, bowel complaints, follow-up operations, osteoporosis, infections and ulcers, deep vein thrombosis, stomal stenosis, and cholelithiasis, among other chronic conditions. The last surgery performed is a liver transplantation in fully cirrhotic patients with liver failure.

Naturopathic/Alternative Care

The best regimen to control insulin resistant in our overweight and obese patients is a low-carbohydrate, low-glycemic diet. The recommended diet by the Nutrition and Metabolism Society, it was confirmed to have patients burn more calories in a recent study. This diet consists of:

1. few or no grains — patients can eat shiratoki noodles, alternative grains made from almond flours, flax crackers;
2. vegetables — excluding the high-carbohydrate ones such as potatoes, sweet potatoes, yams, carrots;
3. some fruit, excluding bananas and focusing on berries;
4. proteins – beans/peas/legumes, seeds/nuts, non-GMO soy, omega-3 organic eggs, grass-fed-finished organic animal products, fish (excluding the ones on the Environmental Working Groups toxic list), organic dairy and alternative unsweetened dairy products;

5. oils: organic butter, unrefined organic olive oils, unrefined organic coconut oil, monounsaturated high oleic safflower oil, avocado oil, walnut oil, flax oil (raw). The focus should be on increasing omega-3 oils, from leafy greens, walnuts and walnut oils, flax seeds and flaxseed oils, oily fish, omega-3 eggs, grass-fed and finished organic meal and poultry;

6. beverages: water, herbal teas, green/black tea, sparkling water, coffee or coffee substitutes, green/vegetable juices, protein smoothies, unsweetened alternative milks (soy, almond, hemp, coconut, hazelnut).

7. sweeteners: stevia, erythritol, xylitol (found in beverages such as Zevia, Virgil’s Zero, Blue Sky Free)

Diets high in saturated fat, soft drinks, and meat, and low in fruits, vegetables, antioxidants, and omega-3-containing fish increase the risk of developing NAFLD/NASH.15

Due to the liver inflammation, absolutely no alcohol can be ingested. Alcohol intake is the largest abuser of the liver and expedites further degeneration and damage. Other foods to avoid include the obvious: refined sugar, particularly high-fructose; fast foods; very processed foods; excessive caffeine. Foods to increase include the cruciferous vegetables: broccoli, cauliflower, brussels sprouts, cabbage, kale, and so on, which with their elevated sulfur content promote detoxification of the liver. Also, the liver responds positively to “bitter” foods, such as arugula, cauliflower, chicory (in coffee substitutes), and dandelion greens, which should be included in the diet as well. Hydrotherapy techniques such as castor oil packs over the liver area as well as “constitutional hydrotherapy” as created and used by naturopathic physicians are also highly recommended.

Exercise is required to encourage weight loss, lower glucose and lipid levels, decrease insulin resistance and hyperinsulinemia, help sleep, improve mood, and increase bowel movements. Exercise lowers the risk of NAFLD, by reducing hepatic triglyceride concentration.16-18 One hour five days a week of mixed aerobic with resistance/weight work is suggested. Physicians need to analyze if their patients need a cardiac evaluation before engaging in exercise. Personal trainers should be used to help learn proper ergonomics with the weight machines.

Sleep is vital. A NHANES study showed that the risk of obesity increased 235% for those who did not get more than 5 hours of sleep a night.19 Also, if patients are not sleeping well or are very tired all day long, a sleep apnea study should be considered. Sleep has a marked effect on appetite-controlling hormones. Having the patient get 7 to 9 hours of good sleep each night lowers ghrelin, a hormone associated with an increased appetite for carbohydrates, so that patients eat less in general and do not crave carbohydrates. It increases leptin, a hormone which lowers the appetite, so that patients naturally desires to eat less. It lowers cortisol, which reduces the risk of abdominal weight gain.

Given the analysis of a patient, an investigation into how “toxic” he or she may be is a good idea. Chemicals known to cause insulin resistance include bisphenol A, Teflon, and phthalates. Arsenic and lead have been shown by the WHO to cause insulin resistance.20

Other analyses are recommended. Checking vitamin D3 levels is good, as well as F/T testosterone, particularly in middle-aged men on statin drugs, in whom studies have shown that statins lower testosterone production. Also, a thyroid panel including TSH, FT3, FT4. And a saliva analysis of morning, noon, afternoon, and evening cortisols and DHEA-S could be helpful, although since abdominal weight produces intracellular cortisol, which may have some systemic effect, cortisol measurements may not really be able to discern abdominal vs. adrenal hypercortisolism.

There are many supportive supplements used to help the liver when it is fatty and inflamed. Supplements can have many benefits such as:

- support for correcting nutrient deficiencies
- support for encouraging weight loss
- antioxidant and anti-inflammatory protection
- appetite control
- support for lowering glucose and insulin
- support for lowering hypertension and lipids
- decreased risk of diabetes and diabetic complications

In general, supplements should help reduce insulin resistance and provide antioxidant protection as two main treatment foci.

Supplements associated with reducing insulin resistance include:
1. chromium: 200–1200 mcg/day
2. zinc: 15–50 mg/day
3. vitamin D: as per individual requirements
4. increased fiber
5. Gymnema sylvestre
6. Momordia charantia

Supplements associated with protecting the inflamed liver by reducing AST/ALT, inhibit cytokine expression, inhibiting fibrosis, inhibiting mitochondrial injury, preventing lipid peroxidation:
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1. R-alpha lipoic acid\(^2\): 600–1000 mg/day; also reduces insulin resistance
2. selenium\(^2\): 200–600 mcg/day
3. milk thistle\(^2\): 200–400 mg/day\(^2\)
4. N-acetylcysteine: 1200–1800 mg/day; also reduces insulin resistance
5. mixed carotenoids, mixed vitamin E, vitamin C
6. probiotics
7. licorice
8. curcumin and resveratrol
9. green tea\(^24,25\)
10. Cordyceps sinensis\(^27\): 1 g three times a day\(^21-27\)

Patients should be clearly told that NAFLD and NASH are reversible liver conditions. No one has to develop cirrhosis from them, ever. Losing the weight is the first and foremost methodology for curing these conditions. Ensuring that the weight loss is slow and antioxidant protection is well established are vital aspects of a safe and responsible treatment program. Follow-up proof of improved conditions. No one has to develop insulin resistance.

Notes
15. de Alwis NMW. Op cit.
27. Mycology News. 1(9).

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