NAFLD / NASH

What Is It?
Non-alcoholic fatty liver disease (NAFLD) describes a spectrum of chronic liver disease in people who drink little to no alcohol. The first stage of this disease involves a buildup of fat in the liver, also known as fatty liver, or steatosis. In some people, this fat accumulation causes inflammation and scarring, or fibrosis, at which point the condition is considered non-alcoholic steatohepatitis (NASH). This inflammation can lead to severe scarring of the liver if enough tissue is damaged—yet another condition known as cirrhosis. (See the Cirrhosis section for more information.) If enough of the liver is damaged from scarring, liver failure could occur. This entire spectrum of liver disease is known as NAFLD.

It has recently been recognized that NAFLD may lead to the development of cardiovascular disease (CVD). This occurs for a couple of reasons. It has been suggested that NAFLD may directly cause atherosclerosis and vice versa, in addition to the ability of many of the individual risk factors of NAFLD, themselves, to lead to CVD.

What Causes It?
In NAFLD the liver has trouble breaking down fats which results in a buildup of fat in the liver. There are many different factors which play a role in the development or worsening of NAFLD. These include:

- Obesity
- Metabolic syndrome
- Insulin resistance
- Type 2 diabetes
- High triglycerides
- High cholesterol
- Oxidative stress
- Dysbiosis
- Leaky gut
- Inflammation
- Candida overgrowth
- Gluten sensitivity / celiac disease
- Milk (casein) allergy
- Poor diet
- Toxins
- Certain medications
- Family history and genetics

Obesity is a major risk factor in the development of NAFLD. In fact, 90 percent of obese people may develop chronic liver injury. It is thought that obesity is the most common cause of NAFLD. Since the obesity rate in the U.S. has increased so drastically in the past few decades, and is projected to continue increasing, NAFLD is becoming more common, and will likely continue this trend. Abdominal fat is an especially important factor in NAFLD, even in people who are not overweight.
NAFLD is closely related to the components of the metabolic syndrome, most notably insulin resistance, another risk factor for NAFLD, which leads to type 2 diabetes. Some consider NAFLD to be part of the metabolic syndrome. Others view it as a consequence of the metabolic syndrome. Also important are some of the individual components of the metabolic syndrome such as: insulin resistance, abdominal fat, high triglycerides and bad cholesterol (LDL and VLDL), each of which can lead to NAFLD. Insulin resistance causes an increase in the amount of glucose in the liver, which is converted into fat that accumulates there. High insulin levels, which coincide with insulin resistance, also decrease the burning of fat because, when insulin levels are high, the body incorrectly thinks that it does not have enough energy (in the form of glucose), so fat storage is increased as a back-up storage source.

A main feature of NAFLD is oxidative stress, which is a direct result of the excess fat accumulated in the liver. It is thought that oxidative stress is largely responsible for the advancement of fatty liver to NASH and cirrhosis. Oxidative stress causes inflammation which damages the liver. Another contributor would be a lack of antioxidants, which counteract oxidative stress.

Dysbiosis, or an imbalance in the intestinal microbes (bacteria, fungi, parasites), plays an important role in the development of NAFLD. The gut-liver connection is illustrated in a number of ways. One major way in which intestinal dysbiosis leads to NAFLD is when microbial endotoxins (toxins produced by bacteria), such as lipopolysaccharide (LPS), trigger an inflammatory reaction in the liver. Small intestinal bacterial overgrowth (SIBO), which is another term for dysbiosis, has been found in 50 percent of NASH patients. The dysbiosis itself leads to a condition known as increased intestinal permeability, or leaky gut syndrome, promoting the ability of partially undigested food particles and toxins (both microbial and otherwise) to enter through the compromised intestine and into the blood supply, which flows first to the liver. Leaky gut and dysbiosis are both associated with NAFLD. (See the Leaky Gut Syndrome section for more information on this condition.) Maintaining a healthy balance of intestinal bacteria is an important step in protecting the liver from damage.

Inflammation is a major component of NAFLD. Inflammation can occur for a number of reasons. The fat itself, which accumulates in the liver, can cause inflammation. But inflammation can also come from an imbalance, or dysbiosis that begins in the gut. The most prominent inflammatory chemical associated with NAFLD is tumor necrosis factor alpha (TNF-alpha). TNF-alpha is involved in all stages of NAFLD. Interestingly, TNF-alpha is produced in large amounts in response to endotoxins, like LPS, produced by bacteria. This further supports the gut-liver connection.

Overgrowth of the intestinal yeast Candida may also be at the basis of liver damage, via leaky gut. Candida overgrowth is a form of dysbiosis, largely caused by one organism, the yeast Candida albicans. An interesting connection to NAFLD occurs when Candida organisms ferment simple sugars in the gut into alcohol. This is also known as “auto-brewery” syndrome. Other pathogenic bacteria are also able to produce alcohol in the gut. The alcohol can contribute to oxidative stress in the liver. In addition, the alcohol can further oxidize to acetaldehyde at toxic levels, contributing to the development of leaky gut and further liver toxicity. Indeed, obese women with
NASH have been found to have increased breath-alcohol levels without having consumed alcohol. This is said to be due to intestinal bacterial overgrowth. Given the fact that alcoholic fatty liver disease involves the same disease process as non-alcoholic fatty liver disease (NAFLD), it is not surprising that an internal production of alcohol by dysbiotic microorganisms is involved in NAFLD.

Gluten sensitivity, or the more advanced celiac disease, may also contribute to the development of NAFLD, again by way of leaky gut syndrome, similar to dysbiosis. Gluten sensitivity involves the inability of the body to completely digest gluten. The body becomes sensitive to the gliadin protein, a component of gluten. This sensitivity involves an immune response against the gliadin, which results in inflammation inside the intestine. This inflammation destroys the lining of the intestine, creating a leaky gut. The partially digested gluten can then enter the bloodstream through the leaky gut, and the inflammatory immune response continues in the bloodstream and into the liver where liver damage occurs as a result of inflammation.

Liver abnormalities are common in people with celiac disease—over 40 percent have increased blood levels of the liver enzyme transaminase. This is a common finding in NAFLD and other liver diseases. In patients with celiac disease who follow a gluten-free diet, these enzyme levels return to normal. Within a year of following a gluten-free diet, 75 to 95 percent of patients with celiac disease were found with normalized liver enzyme levels. Even in severe liver disease, a gluten-free diet has been shown to prevent liver failure.

In addition, milk allergy can also cause liver damage by way of a leaky gut. It may be that the most important part of these processes is the leaky gut, since it allows the entrance of excess toxins into the liver. Maintaining a healthy intestinal lining is a critical part of supporting liver health.

Poor diet is also involved in the development of NAFLD. This is illustrated by the fact that obesity and insulin resistance, both largely due to poor diet, are main factors contributing to NAFLD. But poor diet may be a factor even if obesity or insulin resistance are not taken into account. For example, a diet which included a high intake of meat and soft drinks and a low intake of omega-3 fats was found in NAFLD patients, even with normal body mass index (BMI).

Like the endotoxins produced in the gut, toxins that are ingested (exotoxins) also adversely affect the liver. The liver functions to detoxify and rid the body of toxins. When the liver is overburdened, whether from an excessive amount of toxins or from a buildup of fat and the ensuing inflammation, the function of the liver becomes compromised. Humans encounter many more environmental toxins on a daily basis than they did in the past, so the liver is working harder than ever. Lessening this toxic burden is an important step in supporting optimal liver health.

Certain medications may cause NAFLD. Some of these include:

- Glucocorticoids (steroids)
- Synthetic estrogen
- Aspirin
- Amiodarone
- Tamoxifen
- Tetracycline
- Methotrexate
- Perhexilene maleate
- Antiviral agents
Family history of diabetes or NAFLD may be found in NAFLD patients. Where specific genes are concerned, certain gene polymorphisms are thought to be associated with the progression of fatty liver to NASH.\textsuperscript{31} This is currently being studied. Environmental influences seem to play the major role in NAFLD development, however.

**What Are the Signs and Symptoms?**

In most people, NAFLD does not move past the fatty liver stage, which is usually not associated with any symptoms. However, some people do experience the following symptoms:

- Fatigue
- Weight loss
- Upper right abdominal pain or discomfort

**How Is It Diagnosed?**

Tests used to help diagnose NAFLD include:

- Blood tests – liver function tests, and to rule out viral hepatitis
- Imaging tests – ultrasound, CT scan, MRI
- Liver biopsy – tissue sample of liver

Since there are no specific tests for NAFLD, diagnosis is partially based on the exclusion of other liver diseases.\textsuperscript{34} Liver function abnormalities, particularly increased transaminase levels, are the first sign of NAFLD, but further testing is needed to confirm NAFLD because increased transaminase levels may be found in other liver diseases, and normal transaminase levels can be found in NAFLD.\textsuperscript{35} Ultrasound is usually the next step because it is a relatively harmless test which can show liver fat accumulation. CT scan or MRI may be preferred in some cases, however. The liver biopsy is the best test for confirming NAFLD. It can also detect the severity of the disease.\textsuperscript{36}

Natural health practitioners may also suggest a comprehensive stool analysis (CSA) (see the Appendix) that can be helpful to determine underlying causes of fatty liver such as bacterial imbalance, fungal infection or yeast overgrowth.

**What Is the Standard Medical Treatment?**

There is really no standard treatment for NAFLD. Treatment depends on the contributing factors for the individual patient. The following recommendations are made according to the patient’s history:

- Lose weight – when obesity is a factor
- Healthy diet – this is recommended for everyone
- Exercise – to encourage overall health
- Control diabetes – when diabetes is a factor
- Avoid toxins – this will help to protect the liver and is recommended for everyone

In overweight and obese people, gradual weight loss can help to reduce liver enzyme levels and insulin levels.\textsuperscript{37} Rapid weight loss, however, can be detrimental, as it may worsen liver disease.

Drugs may be prescribed depending on what factors underlie each patient’s NAFLD. Medications to treat insulin resistance may be prescribed, as well as medications for lowering triglycerides or cholesterol.

In the most severe of cases, liver transplant may be necessary, but, even in these cases, NAFLD may develop in the transplanted liver.\textsuperscript{38}
There are approximately 70 million Americans with NAFLD (non-alcoholic fatty liver disease) and about 20 percent of them have NASH (non-alcoholic steatohepatitis) which translates into about 14 million Americans who will likely end up with cirrhosis due to chronic liver inflammation leading to either liver transplant or death. These conditions are already at epidemic proportions, and will bankrupt the country and overload the operating rooms if we don’t change our diet, sleep, and exercise, improve elimination, and decrease stress and toxic exposures.

It is interesting that the medical profession has chosen to call fat in the liver NAFLD or NASH (NAFLD often progresses to NASH). I guess it is nice to know alcohol doesn’t have anything to do with it, since that creates enough problems on its own. However, the diet that creates NAFLD/NASH can be as dangerous as too much alcohol. An acronym that would better state the truth would be BDBBTLSFLD. I know it’s a little long, but it tells it like it is; Bad Diet, Bad Bacteria, Terrible Life Style, Fatty Liver Disease (Bad Diet Disease for short). Bad Diet Disease includes too much of the following: saturated and trans-fats, simple carbs such as: white pasta, bread, cereal, excess sugar (it’s in everything), liquid sugars in soft drinks, sugar- and fat-loaded coffee, junk snack foods, candies, and desserts loaded with high fructose corn syrup. Remember that your mitochondria breathe in your oxygen to make ATP for you, which is your energy currency. If you choose to eat a diet with excess saturated fats, your mitochondria are likely to make excess hydrogen peroxide and damage themselves, thereby knocking out your own energy and your ability to function normally or to repair anything.

The Bad Diet is one of the best ways to increase total body inflammation which, in turn, promotes fat storage. Fat produces at least 10 hormones which are released and cause more inflammation, creating a vicious cycle that promotes further fat storage. When fat storage is excessive, it may first fill the fat cells (adipocytes) under the skin in the abdominal cavity. The extra fat in the blood (in the form of free fatty acids) can then be stored in cells of the muscles, pancreas, heart, blood vessel walls, and liver. Fat in these cells may seriously disrupt normal function, which is known as lipotoxicity. In other words, high blood levels of free fatty acids...
are converted into increased intracellular triglycerides that crowd the cell and create chronic cellular dysfunction and injury. This process can account for many manifestations of the metabolic syndrome, which often leads to NAFLD.

Bad bacteria, or just too much bacteria, especially in the small bowel, are also a major factor in increasing hepatic free radicals and inflammation leading to NAFLD/NASH. There are studies that have shown both increase in intestinal permeability and small intestine bacterial overgrowth (SIBO) in patients with NAFLD and NASH. Overgrowth of Candida and bacteria in the gut produces alcohol which is easily converted into acetaldehyde which travels from the gut to the liver through the portal vein and creates cellular changes like that seen with NAFLD.

Another bacterial connection involves eating a high-saturated-fat diet which causes the intestinal bacteria to release their cell wall lipopolysaccarides (LPS), as well as other endotoxins. Their first stop is the liver where they create inflammation, and then on to the entire circulation where they create endothelial dysfunction (blood vessel wall dysfunction, and leaking), creating the so called "leaky vessel" syndrome.

As one might expect, treating with probiotics has been shown to improve NAFLD and lower NF-kB activity (major nuclear transcription factor for inflammation) after four weeks of therapy.

Early diagnosis and treating people with the correct diet and life style changes is essential. In addition to being overweight with a large belly (waist/hip ratio less than 0.8 for women and 0.9 for men), an abdominal ultrasound or an MRI spectroscopy will usually make the diagnosis of fat in the liver. The blood tests include: cholesterol/HDL, triglyceride/HDL, and apo B/apo A-I ratios. These ratios give a clearer view of the overall lipid status of the patient, and serve as tools to monitor progress with diet and lifestyle changes. The lifestyle changes include exercise, stress reduction, sleep, proper elimination, appropriate supplementation with extra antioxidants, and detoxification. These will be essential if we are to reverse this epidemic.

Since some people may not be clearly overweight, and many overweight people may not have NAFLD/NASH, it is important to do the blood tests and check the blood pressure for early signs of the conditions. The pattern follows closely to that of metabolic syndrome and type 2 diabetes with: high blood pressure, abdominal obesity, high cholesterol, triglyceride and LDL, low HDL, lipoprotein imbalances, and elevated blood sugar and/or insulin levels.

As soon as it is apparent that the patient is headed toward metabolic syndrome or NAFLD/NASH, the diet should be changed. There is data to support the DASH diet or the Mediterranean diet, which includes: vegetables, whole fruit, whole unprocessed grains, legumes, low sodium foods, lean cuts of meat and fish, and increased omega-3 fatty acid intake and olive oil, may alone reverse the problem if done early enough. The HOPE program would also play an important part here with high fiber, essential oils with the right balance of omega-6/omega-3, probiotics, and enzymes. Omega-3 and 6 fats help to remove liver fat through speeding up metabolism.

However, if the person waits too long, and has gone too far with advanced metabolic syndrome, and dangerous levels of NAFLD/NASH, pharmaceutical drugs or gastric bypass will be necessary to prevent progression to cirrhosis.
In my experience, people who have fatty liver also have a major Candida overgrowth that compromises the liver. This gut imbalance created by Candida overgrowth results in an overburdened liver because toxins from the gut are transported directly to the liver. I strongly recommend that everyone with this condition follow a complete cleansing program that includes a Candida cleanse, in addition to eating a Candida diet for three to six months. (See the Appendix for more information.)

Fatty liver is one of the gateway conditions between digestive function and other conditions like metabolic syndrome, diabetes and cardiovascular disease. The good news is that this condition can be reversed. Correcting any digestive dysfunction through diet and supplementation, and maintaining a healthy weight through exercise and lifestyle changes, can go a long way to healing fatty liver, and, thus, preventing these more serious health conditions.

**Recommended Testing**

- Comprehensive stool analysis (CSA) (See the Appendix.)

**Diet**

- Follow the Candida Diet (see the Appendix) for three to six months.
- Next, follow the Fiber 35 Eating Plan. (See the Appendix.) Include plenty of fruits and vegetables.
- Watch protein intake (especially animal sources) if ammonia levels are high. If you do eat animal protein, limit to small quantities of poultry and fish.
- Watch fats, especially fried foods, saturated and trans fats. If the liver is too damaged, it may not be able to handle fat-soluble vitamins like A, D, E and K, except in small amounts.
- Keep refined carbohydrates (sugar, white bread, white pasta, white rice, etc.) out of your diet. Carbohydrate consumption should be in the form of vegetables and whole grains.
- Do not overeat. Eat small meals more frequently.
- Do not consume alcohol (most important!).

**Lifestyle**

- Medications can be stressful for the liver. Take with caution.
- Do not become constipated. Use the LifeStep (see Resource Directory) for proper elimination posture.
- Do not smoke, and avoid second-hand smoke.
- Clean up your environment, as all chemicals and toxins can affect liver function.

**Complementary Mind / Body Therapies**

- Stress can be a major component of this disease, so find ways to reduce it with therapies such as meditation, yoga, deep breathing, massage, biofeedback, or music therapy.
- Colon hydrotherapy is beneficial to remove toxins.
### Recommended Nutraceuticals

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<tr>
<th></th>
<th>Dosage</th>
<th>Benefit</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Critical Phase</strong></td>
<td><strong>Daily maintenance recommendations should also be taken during this phase unless otherwise indicated.</strong></td>
<td></td>
<td></td>
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<tr>
<td>Total Body Cleanse</td>
<td>See Appendix</td>
<td>Encourages elimination and detoxification.</td>
<td>Herbal formula should support the seven channels of elimination.</td>
</tr>
<tr>
<td>Liver Detox</td>
<td>This should follow the Total Body Cleanse. See Appendix</td>
<td>Encourages detoxification involving the liver.</td>
<td>Should contain milk thistle seed extract containing silymarin, phosphatidylcholine selenium and herbs.</td>
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<tr>
<td><strong>Helpful</strong></td>
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<tr>
<td>SAMe</td>
<td>180 mg per day</td>
<td>Helps improve liver function.</td>
<td>Do not use if you have bipolar disorder or are taking antidepressants.</td>
</tr>
<tr>
<td>L-Glutamine Powder</td>
<td>5 grams twice daily</td>
<td>Essential for maintaining the health and integrity of the intestinal lining.</td>
<td>Added gamma oryzanol may help relieve pain associated with gastrointestinal complaints.</td>
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<tr>
<td>with Gamma Oryzanol</td>
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<tr>
<td>High Potency</td>
<td>Follow directions on label</td>
<td>Provides needed nutrients that may be deficient.</td>
<td>Powder or liquid formulation would be helpful as it is easier assimilated and absorbed.</td>
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<tr>
<td>Multi-vitamin/mineral</td>
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<tr>
<td>Antioxidant</td>
<td>Use as directed</td>
<td>Protects tissue from damage.</td>
<td>You can purchase a high-potency antioxidant formulation from most health food stores.</td>
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<tr>
<td>Supplement</td>
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<tr>
<td><strong>Daily Maintenance</strong></td>
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<tr>
<td>Critical Liver Support Formula</td>
<td>Use as directed</td>
<td>Enhances liver detoxification.</td>
<td>Should include milk thistle seed extract containing silymarin, N-acetyl-cysteine, alpha lipoic acid L-glutathione.</td>
</tr>
<tr>
<td>Fiber</td>
<td>4-5 grams twice daily</td>
<td>Helps produce healthy bacteria levels and good elimination.</td>
<td>Use in conjunction with high-fiber diet to reach 35g daily.</td>
</tr>
<tr>
<td>Digestive Enzymes</td>
<td>Take with meals</td>
<td>Helps digest and absorb nutrients from food to reduce liver stress.</td>
<td>If low stomach acid is found, find a formula that contains hydrochloric acid.</td>
</tr>
<tr>
<td>Omega-3 Fatty Acids</td>
<td>At least 2 grams daily of EPA/DHA combination</td>
<td>Reduces inflammation.</td>
<td>Look for a concentrated, enteric coated fish oil.</td>
</tr>
<tr>
<td>Probiotics</td>
<td>30 - 80 billion culture count twice daily</td>
<td>Restores bacterial balance and pH of colon and promotes regularity.</td>
<td>Look for high amount of bifidobacteria, the main beneficial bacteria in colon.</td>
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See further explanation of supplements in the Appendix