Hepatic Fat Metabolism Protocol‡

DEVELOPED IN COLLABORATION WITH OUR SCIENTIFIC AND MEDICAL ADVISORS

This protocol offers diet, lifestyle and supplement recommendations to support optimal metabolic and liver health.‡

FOUNDATIONAL SUPPORT

In addition to a healthy diet and lifestyle, consider the following foundational supplements to support overall health and well-being:

- O.N.E.™ Multivitamin (ONE1 / ONE6 / ONE3)
- O.N.E.™ Omega (ONO6 / ONO3)
- Probiotic 50B (PR56)

FOCUSED SUPPORT

The products in this category support common clinical objectives related to liver heath and metabolism.‡

Choose from the options listed below:

CLINICAL OBJECTIVE‡	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Hepatic Fat Metabolism AST, ALT, GGT and altered fat metabolism in the liver		**Lipid Support Complex** (Order Code: LSC6) Supports hepatic fat metabolism, oxidative stress, vascular health and uric acid levels‡ **ADD** **Choline (bitartrate)** (Order Code: CLB1) Supports healthy hepatic fat metabolism‡	2 capsules daily, with a meal 1 capsules, 1-2 times daily, with a meal
Liver Cell Health	AST, ALT, GGT, environmental toxin exposure	**Silymarin** (Order Code: SL6 / SL1) Milk thistle extract standardized to contain 80% silymarin to support liver health, offers antioxidant support to protect the liver and stimulates protein synthesis in hepatic cells‡	1 capsule, 1-4 times daily, between meals
Glucose Homeostasis	Insulin, HbA1c, Advanced lipid profile	**Berberine UltraSorb™** (Order Code: BUS6) Enhanced absorption berberine to support glucose metabolism, healthy insulin receptor function and metabolic health‡	1 capsule, 1-2 times daily, with or between meals

ADDITIONAL CONSIDERATIONS

The products in this category offer added support for cellular, liver and cardiovascular health. Choose from the options listed below.‡

CLINICAL OBJECTIVE‡	ASSESSMENT*	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Cellular & Antioxidant Support	Whole blood glutathione, GlycA	**NR Longevity™** (Order Code: NRL6) Includes clinically researched NIAGEN® nicotinamide riboside, sulforaphane and trans-resveratrol to help replenish NAD+, enhance mitochondrial function and support antioxidant defenses‡ or **Liposomal Glutathione liquid** (Order Code: LGL) Enhanced absorption liposomal glutathione to support antioxidant defense, detoxification and cellular function‡	2 capsules, 1-2 times daily, with meals 2 pumps by mouth, 2 times daily. Hold in mouth 30 seconds before swallowing. Take on an empty stomach, at least 10 minutes before meals
Cytokine Balance & Liver Cell Health	AST, ALT, Advanced lipid profile, CRP, TNF-α, IL-6, LDL-C	**CurcumaSorb** (Order Code: MCU1) Meriva® bioavailable curcumin phytosome for cytokine balance and cellular health‡	2 capsules, 1-3 times daily, between meals
Healthy Immune Function & Cardiovascular Support	AST, ALT, hsCRP, ApoA, ApoB, MPO	**Garlic Complex** (Order Code: GRC1) Aged fermented black garlic and garlic extract to promote antioxidant defense and support cardiovascular and cellular function‡	2 capsules, 1-2 times daily

Clinical Assessments for Liver Health

- CBC, CMP
- Advanced Lipid Profile
- Conduct initial screening in individuals with metabolic alterations
- Ultrasound or CT imaging if elevated liver enzymes (AST, ALT, GGT) are present
- Exclude significant alcohol use
- Assess risk or development of fibrous tissue with Fib-4 Index, ELF score and GGT levels
- Routinely monitor:
  - CMP with Fib
  - CBC
  - Insulin
  - C-peptide
  - A1C
  - Uric acid (<4.5 mg/dL in women, < 5.5 mg/dL in men)
  - Thyroid panel (TSH, TT3, FT3, FT4, RT3, Anti-TPO, Anti-TPG)
  - hsCRP
  - Ferritin & Iron panel
  - Lipid panel
  - Homocysteine
  - ELF Score, GGT

Altered fat metabolism in the liver affects approximately 25% of the global population, making it the most common health concern affecting the liver.[1] In the United States, prevalence is nearing 40%, a number that has increased by 50% over the last 30 years.[2] Changes in hepatic fat metabolism are experienced more highly among individuals with altered metabolic profiles. Optimal support and risk reduction require early assessment, routine screening in high-risk populations, individualized lifestyle and nutritional strategies, along with continuous monitoring of clinical biomarkers.

DIET AND LIFESTYLE CONSIDERATIONS

Diet and lifestyle changes are highly effective and accessible strategies for supporting metabolic and liver health.

Fructose

Cross-sectional studies have shown strong associations between sugar-sweetened beverage consumption and altered fat metabolism in the liver.[5] Fructose, a monosaccharide implicated in suboptimal liver health, is metabolized almost exclusively in the liver.

High fructose intake bypasses normal appetite regulation in that fructose doesn't stimulate insulin or leptin sufficiently and promotes overeating. Excess fructose dramatically increases de novo lipogenesis (DNL) in the liver, leading to accumulation of triglycerides in hepatocytes.[6] High fructose and sugar-sweetened beverage intake also increase uric acid, contributing to oxidative stress and fatty acid oxidation.[7] Over time, high-fructose diets can lead to changes in liver fat metabolism, insulin signaling and cytokine release.[8]

Standard American Diet

Excess calorie intake – especially from **sugar, refined carbs and unhealthy fats** typical of the Standard American Diet (SAD) promotes weight gain and metabolic alterations.

The SAD's typical nutritional profile (high in fructose and saturated fat, low in fiber and antioxidants) is particularly "lipogenic" – meaning it favors liver fat synthesis and storage.[9] Over time, this dietary pattern can induce oxidative stress and immune pathways in the liver.[9]

Changes in insulin signaling, often triggered by refined carbohydrates, high-glycemic diets and excess visceral fat, further exacerbate changes in fat metabolism in hepatocytes and immune activation.[10]

Lack of dietary fiber means less satiety and impaired gut barrier function, potentially increasing endotoxin absorption that can worsen hepatic immune response.[10]

The Standard American Diet, rich in fructose, refined carbs and saturated fats, impacts how the liver processes fat. In contrast, diets with low glycemic load, abundant fiber and unsaturated fats tend to mitigate these unfavorable processes.

The Mediterranean Diet

Often cited as a ***protective*** dietary pattern against metabolic alterations, the Mediterranean diet has been shown to reduce hepatic fat and improve insulin sensitivity, even without weight loss.[11]

The Mediterranean diet has multiple components beneficial for liver health, including high fiber and antioxidant content, a low glycemic load and healthy fats that improve lipid profiles and vascular health.

DIET AND LIFESTYLE CONSIDERATIONS *CONTINUED*

The Mediterranean diet is characterized by:

- **High intake of plant-based foods:** vegetables, fruits, whole grains, legumes, nuts and seeds (rich in fiber and antioxidants)
- **Olive oil as the primary fat source:** high in monounsaturated fats and polyphenols
- **Regular consumption of fatty fish and seafood:** a key source of omega-3 polyunsaturated fats
- **Moderate consumption of dairy (cheese, yogurt) and wine (red wine in moderation with meals)**
- **Low intake of red and processed meats, sweets and saturated fats**

By addressing metabolic risk factors, the Mediterranean dietary pattern indirectly alleviates some of the underlying drivers of changes in liver health.

Clinical Action for Dietary Recommendations	**Diet**
	Encourage 5-10% weight loss in overweight individuals, and maintain a healthy weight with habits that include:
	• Consistent and early-day meal consumption, emphasizing breakfast
	• Discourage late-night eating and fluctuating mealtimes
	• Promote regular meal frequency
	• Consider personalized protocols of time-restricted eating (8, 10, 12-hour windows)
	• Emphasize the importance of a whole foods, low-glycemic and phytonutrient-rich Mediterranean-style diet comprised of a high intake of:
	  • Vegetables
	  • Fruits
	  • Fatty fish
	  • Nuts and seeds
	  • Legumes
	  • Whole grains
	  • Olive oil
	• Encourage at least 25 grams of fiber daily to support production of beneficial short-chain fatty acids (e.g. acetate, propionate and butyrate)
	• Recommend patients avoid alcohol, high sugar, fructose and high fat foods

EXERCISE

Sedentary behavior is a contributor to excess weight and poor metabolic health outcomes. Both aerobic and resistance training have been shown to provide metabolic benefits even without significant weight loss.[12] Both forms of exercise reduce intrahepatic lipids. Aerobic exercise can also reduce ALT and AST, and resistance training can lower total cholesterol and triglycerides.[12]

Clinical Recommendations for Exercise	**Physical Activity**
	• Inform patients of the benefits of regular physical activity that incorporates lifestyle movement, cardiovascular exercise, HIIT resistance training and mind-body practices like yoga. Emphasize:
	  • 150-300 minutes/week of moderate-intensity aerobic exercise
	  • Resistance training 2-3 times per week
	• Encourage personalized exercise regimens that consider frequency, intensity and timing to improve patient adherence
	• Continue to monitor anthropomorphic measurements and metabolic biomarkers

SLEEP

Sleep is a **fundamental**, yet often underappreciated, determinant of metabolic homeostasis. Meta-analyses of human studies show that **short sleep (<6–7 hours)** is associated with a ~**15–22% increased risk** of altered metabolic health outcomes, with both insufficient (<5.5 h) and long sleep (>9 h) linked to greater prevalence and incidence in some cohorts.[13, 14, 15, 16] Poor **sleep quality**, delayed sleep timing and circadian misalignment further elevate risks of excess weight, changes in insulin responses, elevated blood pressure, altered lipid profiles and systemic immune response.[13, 17]

Clinical Recommendations for Sleep	**Sleep** • Incorporate sleep history screening (duration, quality, bedtime routines) into metabolic risk assessment • Provide sleepy hygiene recommendations

For targeted support related to sleep, refer to

- Sleep Support Protocol‡

CONTRIBUTING FACTORS

Changes in liver health arise from interactions between **metabolic health, thyroid hormones, environmental toxicants** and **iron levels**. These interactions are driven by changes in insulin responses, altered lipid metabolism, oxidative stress and immune activation.

Metabolic Health

Changes in liver health are considered hepatic manifestations of altered metabolic health. Key mechanisms contributing to changes in liver health include:

- Excess visceral fat
- Changes in insulin sensitivity and glucose metabolism
- Changes lipid metabolism
- Diet

METABOLIC FACTORS IMPACTING LIVER HEALTH[18, 19, 20, 21, 22, 23]

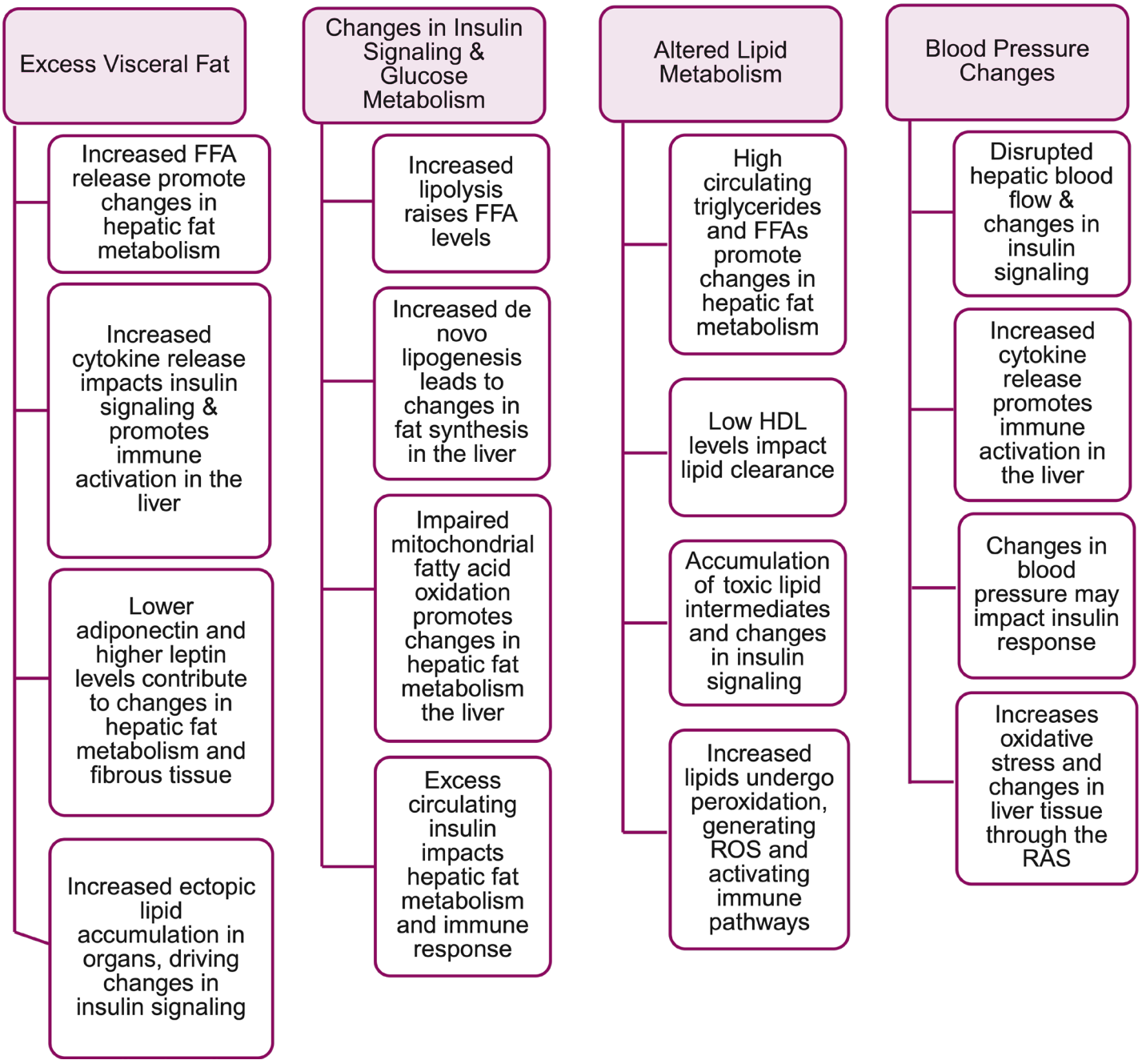

Image created in BioRender.com

FFA (free fatty acid), **ROS** (reactive oxygen species), **RAS** (Renin-angiotensin system)

For targeted support for cardiometabolic health refer to:

- Cardiometabolic Support Protocol

Thyroid Hormones

Thyroid hormones, particularly T3 and T4, play a pivotal role in regulating lipid metabolism, energy expenditure and hepatic function. When low T3 levels or altered Free T3/Free T4 levels exist, these regulatory pathways are disrupted.[24]

Altered thyroid function impacts lipid metabolism by reducing LDL receptor expression and hepatic lipid clearance. It can impact glucose uptake, insulin sensitivity and promote gluconeogenesis. Thyroid hormone imbalance also drives oxidative stress and cytokine release, while disrupting adipokine profiles – lowering adiponectin and elevating leptin and resistin. These metabolic and immune changes promote fat accumulation, immune activation and development of fibrous tissue in the liver.[24]

Practitioners should routinely assess thyroid function in patients with or at risk of altered fat metabolism in the liver and consider targeted support for thyroid health.

Gut Microbiome

An imbalance in the composition and function of the gut microbiota can promote a cascade of physiological changes that culminate in immune activation in the liver.[26, 27]

Loss of Microbial Diversity and SCFA Producers	Increased Intestinal Permeability	Immune Activation in the Liver

• ↓ Diversity of gut microbes
• ↓ Short-chain fatty acid (SCFA)-producing bacteria
• ↑ Firmicutes/Bacteroidetes ratio
• ↑ Cytokine release
	• Translocation of lipopolysaccharides (LPS) into the bloodstream
	• Circulating LPS triggers an immune response leading to:
	  • ↑ TNF-α, IL-6, IL-1β
	  • ↑ C-reactive protein (CRP)
	  • Recruitment of neutrophils and macrophages
		• Direct exposure to LPS via the portal vein results in:
		  • Kupffer cell activation
		  • Hepatocyte changes
		  • Development of fibrous tissue

Additionally, a meta-analysis of 34 studies involving over 175,000 individuals revealed a significant association between *Helicobacter pylori (H. pylori)* and fat metabolism in the liver. Both were linked to metabolic factors such as BMI, blood pressure, lipid profiles and liver and kidney function, suggesting a shared physiological pathway.[27]

ENVIRONMENTAL FACTORS

Environmental chemical exposure plays a significant role in changes to liver health. Lipophilic toxicants such as industrial pollutants, pesticides and persistent organic compounds accumulate in adipose tissue and disrupt hepatic lipid metabolism, mitochondrial function and immune signaling.[28,29] These chemicals impact detoxification pathways, increase oxidative stress and promote hepatocyte changes, contributing to fat metabolsim in the liver and development of fibrous tissue.

Clinicians should consider environmental exposures as part of a comprehensive assessment of liver health, especially in patients with unexplained metabolic alterations or changes in liver health that are resistant to therapeutic strategies.

IRON LEVEL

Iron is essential for cellular function, however, levels can impact liver health through multiple interconnected mechanisms: [30,31]

1. **Iron Overload**: Excess iron accumulation in the liver contributes to oxidative stress, hepatocyte changes and development of fibrous tissue.
2. **Hepcidin levels** may be altered when changes in fat metabolism occurs in the liver. This imbalance leads to **excess iron**, which impacts the liver and development of fibrous tissue.
3. **Changes to insulin signaling** may influence iron metabolism by promoting hepatic iron deposition and altering ferritin levels. Excess iron may also impact insulin signaling.
4. **Genetic Variations,** specifically mutations in iron-regulating genes, are more prevalent in patients with altered fat metabolism in the liver.

Understanding these mechanisms can help practitioners target interventions and laboratory assessments more effectively and personalize care strategies for their patients.

STRESS AND MOOD

Low mood and occasional anxiety are increasingly recognized as risk factors for impacting hepatic fat metabolism. Several biological mechanisms explain this link. Stress and low mood can disrupt the hypothalamic–pituitary–adrenal (HPA) axis, leading to elevated cortisol levels that drive visceral adiposity, changes in insulin signaling and altered fat metabolism in the liver. These mood states are also associated with systemic immune response, characterized by increased cytokines such as IL-6 and TNF-α and with oxidative stress, both of which contribute to hepatocyte changes and immune activation in the liver.[32] In addition, altered gut microbiota often seen in mood concerns may increase intestinal permeability and endotoxin release, fueling hepatic immune response and impact lipid regulation.[33]

Epidemiological studies support this biological connection. Large cross-sectional analyses show that individuals with low mood and occasional anxiety have a higher prevalence of changes in hepatic fat metabolism, with some evidence of a stronger association in women.[34] A recent meta-analysis found that low mood was associated with a modest but significant increase in risk that was not genetically underpinned. Lifestyle behaviors — such as poor diet, reduced physical activity and sleep disruption are linked to both mood concerns and metabolic burden. Together, these findings highlight how mood concerns can act as both biological and behavioral drivers of changes in fat metabolism in the liver, highlighting the importance on working on both mood and liver health for best patient outcomes.

Clinical Recommendations for Stress	**Stress Management** • Assess impact of stress on patient's overall health • Encourage mind-body practices to support resilience and recovery from stress

ADDITIONAL RESOURCES

For additional general recommendations, refer to the following blog posts and protocols from Pure Encapsulations®:

GUT HEALTH

- Nutrient Solutions to Complement the 5R Protocol (Blog)
- Leaky Gut Protocol‡

SLEEP

- Sleep Support Protocol‡

STRESS & MOOD

- Stress Management & Relaxation Protocol‡
- Positive Mood Protocol‡

Available for download at PureEncapsulationsPro.com/Protocols

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