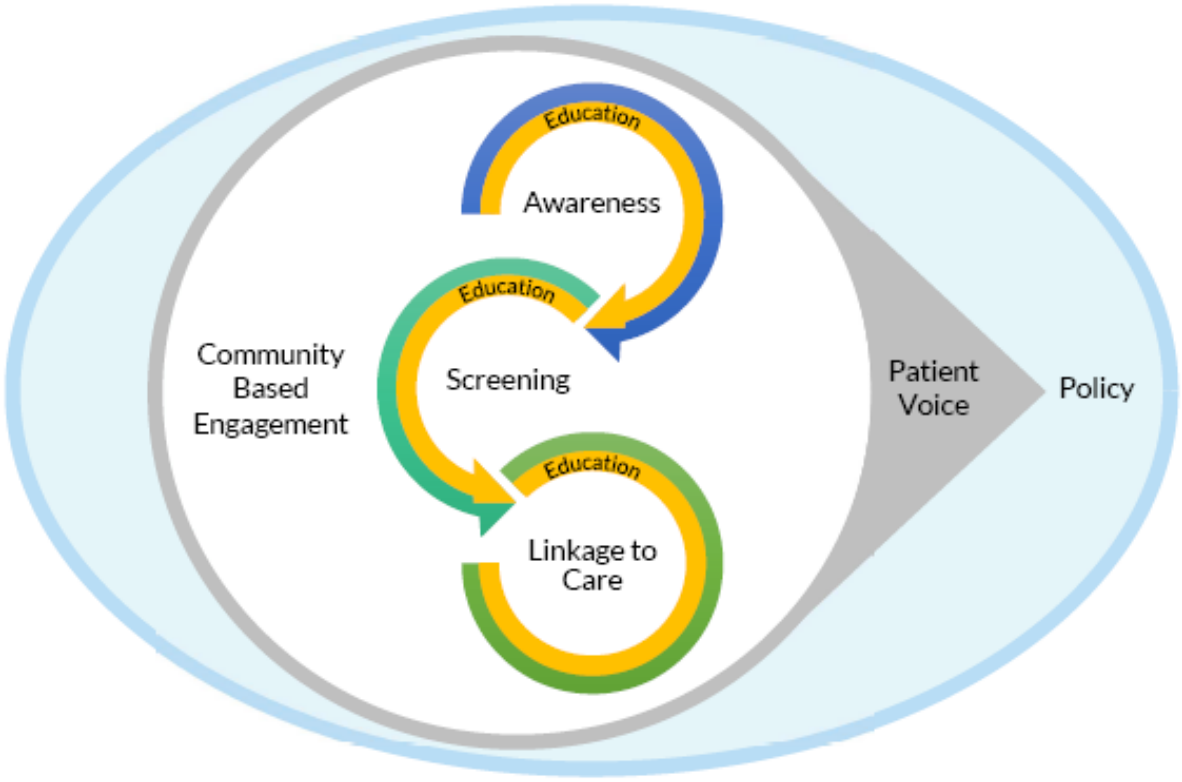
Fatty Liver Foundation



THE LIVER FRIENDLY DIET ™

Managing diet as recommended by the Fatty Liver Foundation

Wayne Eskridge CEO

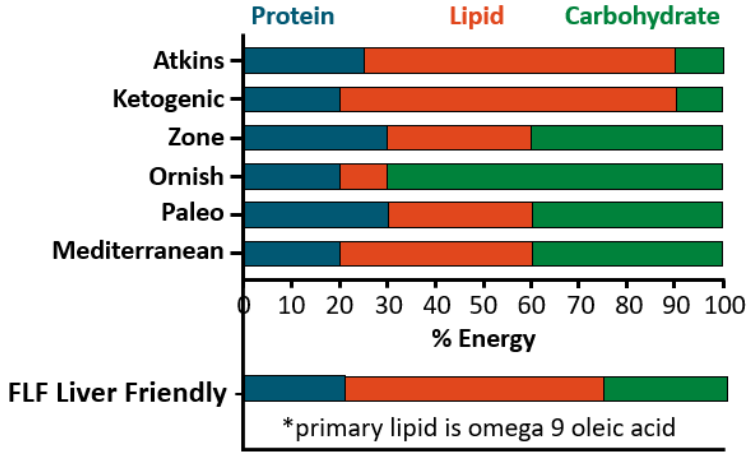
[Date]

Dietary strategies with NAFLD/NASH

Dietary strategies for the management of NAFLD and NASH

OVERVIEW

The Fatty Liver Foundation recommends a diet high in oleic acid (omega 9) unsaturated fat (30%), primarily from extra virgin olive oil, low in saturated and trans fats (7%), with omega 3 and 6 fatty acids approximately equal (8% each). Protein is about 20% of calories and carbohydrates are primarily in the form of fruits, non-starchy vegetables, and whole grains (27%). Simple carbs, such as sugars and refined grains, are minimized. The goal for salt intake is about 70% of the USDA recommendation. Processed foods and red and processed meats are avoided.



Nonalcoholic fatty liver disease (NAFLD) affects approximately one third of adults in the United States and is the most common cause of chronic liver disease worldwide. About 20% of patients develop the more serious steatohepatitis (NASH) which is becoming epidemic as a result of the rising rates of obesity and metabolic disease. Emerging data suggest weight loss of greater than 10% of body weight is beneficial in resolving steatosis and reversing fibrosis due to NASH.

THE PROBLEM: The liver experts don't offer effective advice

Currently the American Association for the Study of Liver Disease (AASLD), the experts who treat liver disease, recommend no specific diet. There are not enough effective clinical trials focused specifically on the liver to give the experts confidence to make that recommendation.

Think of that. The organ experts don't have enough proof that they are willing to endorse a specific diet, so keep that in mind as you listen to sales pitches. There are thousands of claims about food. Here we are trying to give you the most complete picture that we can but just remember, if someone is selling you something, they have an agenda and evidence is hard to get.

As patients where do we look for dietary guidance?

We understand the challenge for science to provide specific and verifiable data, but as patients we still have to live each day and we make decisions about our diet by making use of whatever information is available to us. We also must live within the cultural and food availability situations that we find ourselves.

It is very difficult to do effective random, blinded, controlled trials (RCTs) of the diets of humans. There are myriad ethical and cultural concerns with human experimentation and the human diet is vastly complex within different cultures and practices. In our role as the voice of the patient, we believe that a position of offering very limited guidance is inadequate so we are providing this information as a patient resource for those who seek to understand the components of diet and available research which we believe offers a coherent view from which to make decisions about diet. The goal of our lifestyle strategy is not to diet but to adopt habits that are fundamentally healthy long term and probably contribute to a healthier liver and a better life.

Making the best choices we can with the information we have

A lifestyle that is fundamentally healthy is built on a vast series of small choices made each day over a lifetime. It is a pattern of behavior based upon choices which are, on average, neutral to healthy while minimizing ingesting things that compromise function. There is no one size fits all solution. Human metabolism is quite robust and is able to accept a wide range of inputs and to use them to sustain bodily functions.

In our role as a supporter of people concerned about liver health, our goal is to support a lifestyle which minimizes the work that the liver must do to sustain our lives. Conceptually, when any of the parallel processes taking place within a liver cell is either oversupplied with or denied those dietary elements that it needs to maintain a stable response we have failed in that goal. In making decisions about food, the goal is stability of function, stability of supply, and minimizing toxins. A sick liver benefits from a strategy of making it do as little work as possible.

Talk to your doctor

All patients should discuss dietary strategies with their doctor. This information cannot substitute for guidance by your physician. This material provides research-based information that will help you better understand your doctor's advice but cannot be relied upon for personal health decisions. Information is critical to help plan and implement a strategy to adopt lifestyle change but there is no single solution to decisions about diet and this information is therefore incomplete and may well be proven to be incorrect as research is performed in the future. This discussion provides information from a health perspective broadly which can inform choices about what constitutes a liver supportive diet. A broader benefit is that this approach provides a holistic regimen which benefits many co-morbid conditions such as diabetes and cardiovascular health as well. In many ways, what is good for the liver is beneficial for the body as a whole.

It is important to remember that your doctor probably has little nutrition education. We rely on them, but many are unprepared to really help us with diet decisions. This paper contains references to research which we have relied upon in developing it so you may be able to use it to engage your physician in the science argument about various aspects of diets. The material presented is not exhaustive or necessarily authoritative but is a coherent way to approach the lifestyle challenge.

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THE SUPPLY BALANCE THEORY OF LIVER HEALTH

This document will discuss diet from a system/energy point of view. An engineering perspective to shed light on how diet is managed by the body. Your physicians and nutritionists won't speak to you this way. Even if they study it, they often don't feel they have the time to spend with you and most doubt that you have the interest or background to think much about the details. If all you want is a cookbook this material probably isn't right for you. If you want to treat your liver kindly the details matter so we invite you to continue.

You, as an individual, know that it is important to have some balance in your life. Constant high-pressure work with no breaks will probably ruin your health. The Fatty Liver Foundation believes that one key to liver health is also to avoid forcing your liver to work very hard all the time.

Our bodies are remarkable. Our internal chemistries have to stay in a fairly narrow range, or we die, and yet we are able to eat a wide range of things without difficulty. The various organs of the body require a lot of different kinds of molecules to function and the liver is involved with most of them, but the key demand is energy. The brain needs glucose or ketones for fuel as one example and the heart utilizes mostly fat. These two organs primarily define your ability to live but they use completely different fuels. You might wonder how that works.

Clearly all of your energy comes from your food. If you eat mostly carbs your liver will make fat. If you eat mostly fat your liver will make glucose and ketones. If you don't eat anything your liver will eventually convert your muscles to the fuels that it needs to support life and will thus consume your body in its effort to keep you alive. Remember, it is balancing the continuous immediate needs of all your organs even though you feed it with large piles of mixed foods from time to time. The fact that we are able to live at all is amazing, but our ability to mostly ignore our internal functions and to abuse them routinely without obvious immediate consequences borders on miraculous.

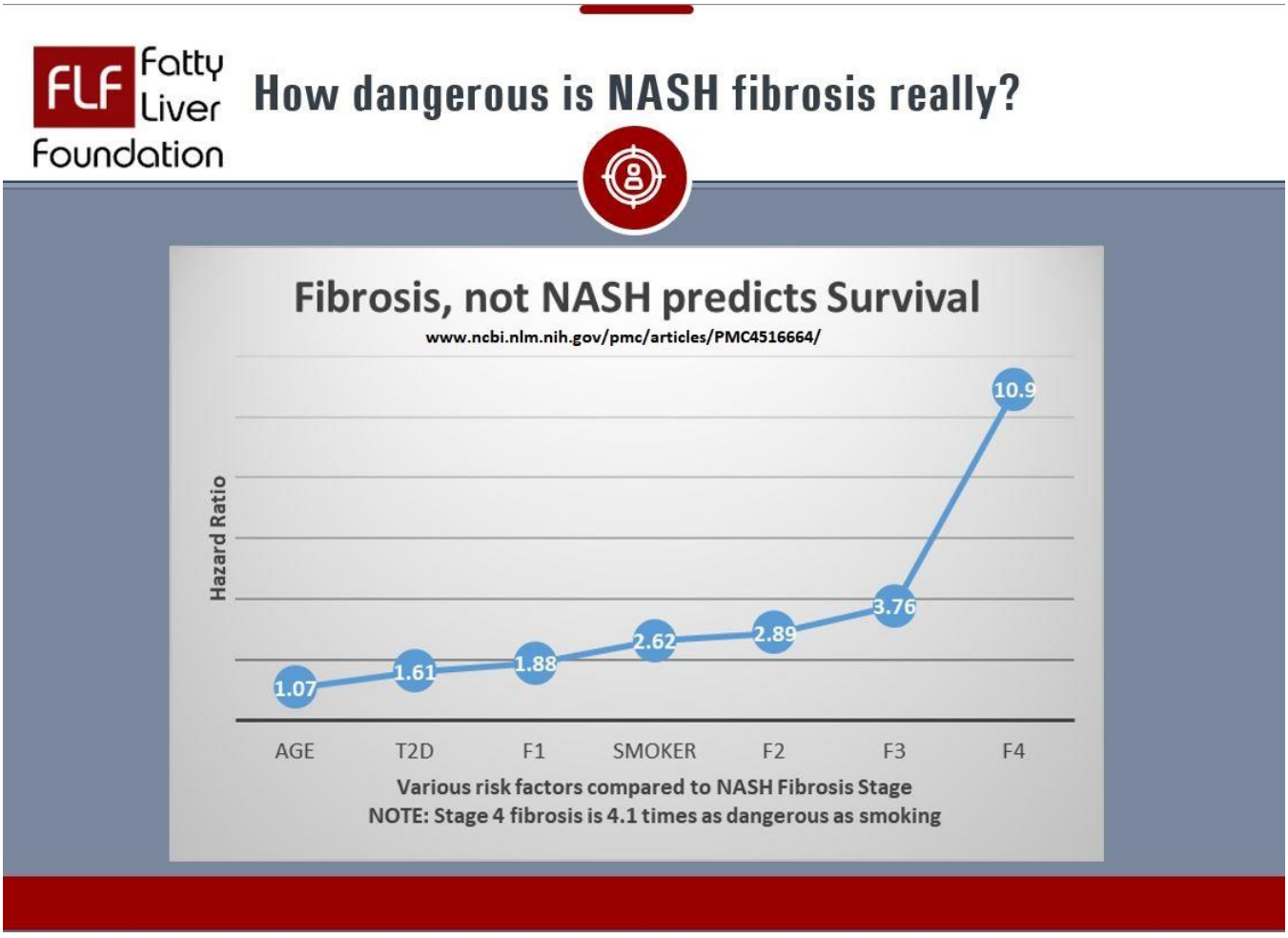
However, just as you can work your body literally to death, with persistence, in a few decades you can work your liver to death. The chemistry within the cell is very robust, but like any system continuous stress causes damage to accumulate and for the liver that often shows up as scar tissue as cells die faster than the processes that clear up dead cells can manage. This leads to the accumulation of wound healing polymers. We call that fibrosis, and in its advanced form cirrhosis, which is scar tissue displacing liver cells. As damage increases the liver gradually stops being able to do its job resulting in liver failure and death.

The strategy behind the Liver Healthy Diet is to use food in a balanced way and thereby to ask the liver to do as little work as possible. The essential point to keep in mind is that the heart and brain, every organ if you wish to be precise, are operating continuously so the liver is constantly managing the demand for glucose and fat quite carefully even though you don't eat carefully and your schedule is highly variable. When supplies are either too high or too low the liver must work harder to keep things running smoothly. A simple concept but the details are vastly complex.

Clearly, the details are complicated. Researchers will focus on that enzyme, this gene, these metabolites, the list is endless when you dive into the details. For you as a patient, however, about all you can control is what you put into your body and hope that it does good things for you or at least doesn't hurt you. The Liver Friendly Diet is a framework to help you understand broadly how the big categories of food, such as fats and carbohydrates, generally interact so that as you consider the details of your diet you can make choices that are on average less stressful for your liver. The fact that this is generally better for your body as a whole is a happy byproduct.

UNDERSTANDING THE HAZARDS OF NAFLD/NASH

The hazard associated with NAFLD/NASH is not well communicated to the public and we face a public health crisis as a result. The lack of wellness screening and early intervention for the disease is well documented but the severity of the risk is not commonly understood by the public or the medical community at large. The typical patient does not learn of their disease until they are at an F3 or F4 stage of fibrosis. By then the risk of death is high and increasing rapidly. **Liver Fibrosis, But No Other Histologic Feature, Is Associated With Long-term Outcomes of Patients With Nonalcoholic Fatty Liver Disease.[1, 2]** Note the chart of hazard ratios, the risk of death, below.



How does the healthcare system manage NASH?

NOTE: In the chart above you can see the hazard ratio for a few problems. The hazard ratio compares your risk of death compared to a healthy person. You can see that stage F1 NASH is more hazardous than Type 2 Diabetes and stage F2 NASH is more hazardous than smoking. We care very much about diabetes and smoking but not very much at all about liver disease absent symptoms. We believe this is a moral failure on the part of the healthcare system. The frequent defense is that since there is no therapy, warning the patient creates needless worry. While it is true that as of this writing there is no pill, but there is ample evidence that weight loss and exercise are effective ways to manage this disease in its early stages.[3] It is also true that the healthcare system does not actively support lifestyle change as therapy. The concept of wellness is embraced by everyone, but the funding and support needed for effective lifestyle change are not available to most patients and wellness is supported as an ideal but is not an effective goal of our healthcare system.

Lifestyle interventions can be highly effective in treating NAFLD across the disease spectrum and offer a holistic way of managing not only liver health, but also cardiovascular and metabolic health. Lifestyle change can be difficult for patients to achieve, but with individualized support, significant long-term changes are possible. **It is critical to understand that if lifestyle change is achieved and sustained, the benefits to liver, cardiac and metabolic health can surpass the efficacy of the drugs currently being evaluated in phase III trials. Thus, lifestyle modification should remain the primary focus for all patients with NAFLD.**[4] While this fact is acknowledged by the healthcare system the structural incentives that exist do not support active engagement with patients seeking to lose weight. Improving that situation is a central challenge of the Foundation.

Here we examine the pathophysiology behind specific dietary components that can either promote or reverse NAFLD to help persons understand our specific dietary recommendations. To date, the data supports reducing saturated fat, refined carbohydrates, and red and processed meats, and increasing the consumption of plant-based foods. [5]

There is a vast array of diet plans, all with sincere advocates. WebMD has a good summary on their website at this link "evaluate latest diets". It is vital to understand that almost any diet plan, if sustained, will result in weight loss. Whether a diet is both healthy and sustainable are crucial issues, but for our purposes, it must also be beneficial to liver health. It is very difficult to do actual controlled feeding trials on diet with human subjects so the data that exists is often with animal models or focused on individual organs or chemistries. As a result, comprehensive authoritative advice is problematic. Most diets address a general audience, but our interest is people dealing with NAFLD/NASH. The standard medical advice is to lose weight and exercise, but little emphasis is placed on how or what kinds of things may be important to consider. This overview seeks to provide a basis for considering lifestyle change from the perspective of first understanding basic metabolic processes as a way to inform individual decisions.

RESEARCH SUPPORTING THE LIVER FRIENDLY DIET

General background overview

The overall evidence in the literature suggests that medium-chain saturated fats (such as lauric acid, found in coconut oil) and monounsaturated fat (oleic acid, found in olive oil) are less likely to promote insulin resistance, inflammation, and fat storage compared to long-chain saturated fatty acids. Examples of long chain fats are stearic acid found in large quantities in butter, beef tallow and particularly in palmitic acid found in palm oil. This benefit is especially true when fats are consumed on top of a diet moderate in refined carbohydrates. Compared to long-chain saturated fats, lauric acid and oleic acid have an increased fatty acid oxidation rate, are more likely to be burned for energy and less likely to be stored in adipose tissue.[6] Omega-6 polyunsaturated fatty acids (PUFAs), such as linoleic acid, as found in vegetable seed oils, may contribute to obesity, whereas omega-3 PUFA may be protective. Importantly, both olive oil as part of a Mediterranean diet, and omega-3 from fish and fish oil have been proven to reduce risk of cardiovascular (CV) events.[7] These relationships have been well developed by heart and diabetes researchers but have not been well developed for the liver. **Since there is no official guidance from the AASLD, we interpret these cross disciplinary results from a liver perspective in the context of diet recommendations.**

It is important to realize that medicine is specialized and operates in mostly narrow lanes. People learn a lot about the heart or brain for example, but only general details on other organs. The primary care doctor is a filter directing people to the specialist that they need. This system naturally developed as too much is known about the details that no one can be an effective generalist today. The result, driven by the press, is that we see headlines about endless medical facts that focus on narrow results. This confuses patients because they have to live with their whole body and can't just be concerned for one organ. Finding a way to live that is, on average, better for all aspects of life is the proper goal.

Medical diet research is very difficult to do broadly. The long time periods involved, and the ethical difficulties is studying humans typically results in the study of specific diseases or organs and advice becomes narrowly focused. As an example, there are thousands of studies that speak to heart disease. That is reasonable since cardiovascular is the leading cause of death, so studies frequently report that some particular food has no heart benefit or is hazardous. For example, in 2005 several studies reported that vitamin E might be hazardous to your health based upon heart studies.[8] Studies in 2018 reported that vitamin E was beneficial in the treatment of NASH and it is the only supplement currently suggested in the management of NAFDL/NASH.[9]

The challenge for patients is that they must make many day to day decisions about diet based upon many competing factors such as food choices available, cultural patterns, personal tastes, family dynamics, and many more. All of this with confusing recommendations from health

researchers. One of the few studies to compare details of many diets in a useful way was done by Zivkovic et al [10] in 2007. The table below is from their report.

This is a very important paper and deserves a careful examination. The work was done a few years ago and various other diets have come and gone since then but understanding the effects of different weight loss programs on things besides weight loss is vitally important. We are awash in a sea of advertising about different weight loss programs. All of them are promising that beach buff body and in fact all of them can promote weight loss. For a patient the question goes deeper because what is important is does the diet promote actual health? If you study the table, it is clear that thinking only about losing weight carries with it other potential risks.

This Table is from a paper called "Comparative review of diets for the metabolic syndrome: implications for nonalcoholic fatty liver disease" by Zivkovic et al [10]

TABLE 1
Effects of diets on selected indexes important to patients with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH)[1]

Diet	Weight	Waist circumference	Steatosis	Insulin sensitivity[2]	DNL	Inflammation[3]	TC	TG	HDL	LDL
USDA	↓	↓			↑		↓	↑		↓
AHA	↓	↓			↑	↓	↓	↑	↓	↓
NCEP Step I	↓	↓		↑	↑		↓	↑	↓	↓
DASH	↓	↓		↑	↑		↓	↑	↓	↓
TLC	↓	↓		↑	↑		↓	↑	↓	↓
American Diabetes Association	↓	↓		↑			↓			
American Dietetic Association	↓	↓		↑			↓			
Mediterranean	↓	↓	↓	↑	↓	↓	↓	↓	↑	↓
Ornish	↓	↓		↑	↑	↓	↓	↑	↓	↓
Atkins[4,5]	↓	↓	↑	↓	↓		↑	↓	↑	↑
Zone[5]	↓	↓		↑				↓		↓
South Beach[4,5]	↓	↓					↓	↓		↓
Weight Watchers	↓	↓		↑	↓	↓	↓	↓	↑	↓

[1] An "up" arrow indicates a likely increase, and a "down" arrow indicates a likely decrease in the index based on studies reviewed in this article. A blank space indicates that there is not enough evidence to predict outcomes. DNL, de novo lipogenesis; TC, total cholesterol; TG, triacylglycerol; USDA, US Department of Agriculture; AHA, American Heart Association; NCEP, National Cholesterol Education Program; DASH, Dietary Approaches to Stop Hypertension; TLC, Therapeutic Lifestyle Changes.

[2] Based on the insulin sensitivity index.

[3] Determined on the basis of plasma cytokine and C-reactive protein concentrations.

[4] This diet may cause rapid or sudden weight loss in the induction period, which may be deleterious in patients with NAFLD and NASH.

[5] This diet may be deleterious in patients with hyperuricemia or kidney dysfunction because of its high protein content.

Implications of the comparative review

This table deserves careful examination. Note that all of the diets examined resulted in weight loss and a reduction in waist circumference. Most improved insulin sensitivity, DNL, and various aspects of metabolic syndrome. The critical information in this review is the steatosis results. Note that most diets had no significant effect on liver fat. Only the Mediterranean diet decreased liver fat while the Atkins diet raised it. To be clear, this work was published in 2007. Since then various diet proponents have adjusted some aspects of their strategy and new programs launch regularly but as a baseline concept these results are instructive and provide conceptual guidance for the strategy the Foundation supports.

Mediterranean diet

A Mediterranean diet rich in extra-virgin olive oil (EVOO) is associated with a reduced prevalence of nonalcoholic fatty liver disease.[11] EVOO is the primary energy source in the dietary strategy of the Fatty Liver Foundation. It has been shown that a Mediterranean diet with extra virgin olive oil of at least 60ml per day reduced the incidence of NAFLD compared to a Mediterranean diet with supplemental nuts or a Mediterranean diet with reduced fat. From a patient perspective an important point was that there were no feeding restrictions meaning it wasn't counting calories. People ate until satisfied and still had the benefit. The excess omega 9 oleic acid in olive oil is a key feature of the diet as overfeeding saturated fat causes distinct effects on liver and visceral fat accumulation which are not present with the unsaturated fatty acid.[12]

Oleic acid an omega 9 fatty acid

Olive oil is about 75% oleic acid which is actually the fatty acid omega 9. Like most fatty acids it is in the form of a triglyceride. We tend to have a negative view of triglycerides because of stories about the harm that they may cause. Much of this negativity is misplaced because of a lack of understanding of fats. Triglycerides are the key energy storage molecule for the body. Triglycerides can't pass through the cell wall of the bowel, so they are broken apart there and the pieces are moved inside the cell then used within the cells of the bowel to build new triglyceride molecules. Fatty acid molecules longer than 14 carbon atoms can't pass directly into the blood stream. Therefore, they are packaged with other molecules and travel through the lymph system so that they bypass the liver initially and can be used by other tissues.[13] Think of that, simple carbs and short chain fats go directly to the liver for processing but longer chain fats go through the entire body first and may enter other cells along the way easing the liver workload. If they do arrive at the liver it may then use them to store as fat deposits or process them into other chemicals that the body needs. It sends surplus to be stored in the fat cells unless the transport molecules are overwhelmed and then the fat stays in the liver promoting a fatty liver or may become the source of other negative processes.

Oleic acid also potently accelerates rates of complete fatty acid oxidation in skeletal muscle cells. This single long chain fatty acid specifically controls lipid oxidation through a signaling/transcriptional pathway. Fatty acids are essential components of the dynamic lipid metabolism in cells. Fatty acids can also signal to intracellular pathways to trigger a broad range of cellular responses. Oleic acid is an abundant monounsaturated omega-9 fatty acid that impinges on different biological processes to modulate rates of fatty acid oxidation. **Importantly, oleic acid, but not other long chain fatty acids such as palmitate, increases the expression of genes linked to the fatty acid oxidation pathway**.[14] It means that there is less oxidative stress in cells using oleic acid as the primary fat source and it is foundational to the diet strategy described here.

The goal of the Liver Friendly Diet

The fundamental strategy is to ask the liver to do as little work as possible. In the context of disease, this allows its natural regenerative abilities to operate most effectively and what processing capacity exists has the best chance to provide critical functions. Since any diet must fit within a culturally relevant context for the individual, we do not provide a list of what to eat or recipes. The goal is to consider all foods in the context of those things that would be more difficult for the liver to manage and to choose accordingly. Broadly speaking **we support a plant-based diet with an emphasis on extra virgin olive oil and omega 3 fish oil as the foundation and not counting calories. A diet built around non-starchy vegetables, whole grains, and adequate protein with a significant fat component rarely leads to hunger distress.**

THE RULE BOOK – THINGS TO CONSIDER WHEN CHOOSING FOOD

What to do to minimize liver risk

- minimize alcohol (ideally eliminate)
- minimize added dietary sugar
- minimize sugar sweetened beverages and fruit juice
- minimize saturated fat and limit red meat
- eliminate high fructose corn syrup
- minimize non-skim dairy products
- eliminate trans-fat (hydrogenated oils)
- limit vegetable seed oils
- limit sodium -- the goal 1,500 mg per day
- minimize simple starches, potatoes, white flour or white rice
- Avoid most supplements except vitamin E
- Make sure that any medications you take are not harming your liver

What to do to maximize food benefit

- Consume mostly unsaturated fats, ideally omega 9, oleic acid
- Consume a wide variety of non-starchy vegetables
- Consume berries, fruits, nuts, and seeds routinely
- Consume whole wheat grains moderately
- Consume protein regularly with an emphasis on plant sources
- Consume fatty fish and other omega 3 sources
- Choose poultry over beef as meat

GENERAL BACKGROUND

"Nonalcoholic fatty liver disease (NAFLD) is defined as the presence of hepatic fat accumulation after the exclusion of other causes of hepatic steatosis, including other causes of liver disease, excessive alcohol consumption, and other conditions that may lead to hepatic steatosis. NAFLD encompasses a broad clinical spectrum ranging from nonalcoholic fatty liver to nonalcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis, and finally hepatocellular carcinoma (HCC). NAFLD is the most common liver disease in the world and NASH may soon become the most common indication for liver transplantation." [15]

Nonalcoholic fatty liver disease (NAFLD) encompasses a spectrum of problems ranging from simple abnormal retention of fat (steatosis) to inflammation of the liver (steatohepatitis). NAFLD is the most common cause of chronic liver disease worldwide, affecting about 25% of the adult population.[16] Approximately 25% of persons with NAFLD have progressed to having cell damage in the liver called NASH (nonalcoholic steatohepatitis), which is associated with a 20% risk of progression to scarring and permanent damage (cirrhosis). It is estimated that NAFLD affects up to 70% of persons with type 2 diabetes (T2D). It affects up to 67% of adults with a body mass index (BMI)[17] between 25 and 30. For BMI greater than 30 it is nearly universal.[13]

Up to 91% of disease results from a surplus of free fatty acids (FFAs) either from excessive formation of triglycerides (lipolysis) 60%, production of FFAs by the liver which is called de novo lipogenesis (DNL) 25%, or from dietary FFA 15%. When coupled with inadequate export from the liver of the triglycerides by very low-density lipoprotein (VLDL), or impaired energy production through fat utilization (beta-oxidation), [18] the result is excess FFAs being stored as triglycerides in the liver cells (hepatocytes). In NAFLD, the storage of FFA (lipolysis) in tissues outside the liver is often resistant to insulin, further increasing serum FFA levels.[19] The accumulation of toxic lipids, along with oxidative stress and a pro-inflammatory environment in the liver, can then lead to NASH.[20] Current dietary recommendations for NASH are for weight loss of greater than 10% of total body weight, which is associated with resolution of steatohepatitis and scar tissue (fibrosis) regression.[21]

"To better understand considerations for adopting a diet plan, the mechanisms of action (pathophysiology) behind how the quality of proteins, carbohydrates (CHOS), and fats can promote or reverse NAFLD is critical."[5]

FEEDING STRATEGY OVERVIEW

The Mediterranean diet, which is similar to the liver healthy diet suggested by the Fatty Liver Foundation is one of the most studied diets in science and medicine. While robust clinical trials are

lacking there is a growing consensus about what constitutes a healthy diet in the context of placing as little burden on the liver as possible and include five key dietary recommendations:[22]

1) Follow traditional dietary patterns, such as the Mediterranean diet;

2) limit excess fructose consumption and avoid processed foods and beverages with added fructose; This is best accomplished by eliminating sugar sweetened beverages;

3) Unsaturated fatty acids, especially omega-9 (oleic acid such as extra virgin olive oil), long-chain omega-3 rich foods and MUFAs, should replace SFAs in the diet;

4) Replace processed food, fast food, commercial bakery goods, and sweets with unprocessed foods high in fiber, including whole grains, vegetables, fruits, legumes, nuts, and seeds;

5) Avoid excess alcohol or ideally eliminate it

Improving diet quality may reduce the incidence and progression of NAFLD and associated risk factors. Many of the benefits are likely to result from the collective effect of dietary patterns. [22-24]

In numerous studies, the Mediterranean diet has been reported to have a beneficial effect on cardiovascular risk factors. The Mediterranean diet was found to be more effective for reducing weight, BMI, waist circumference, inflammatory markers, glucose, total cholesterol, triacylglycerol, and insulin resistance, increasing HDL, improving endothelial function, and reducing the prevalence of the metabolic syndrome compared with the low fat control diet. Taken together, these results suggest that relatively high dietary fat intake, in itself, is probably not associated with accumulation of fat in the liver or other cardiovascular risk factors, and that the type of dietary fat (saturated fat, monounsaturated fat and polyunsaturated fat) may be more important than the amount.[12, 25-28]

The Mediterranean diet is characterized by a high consumption of fruit, vegetables, legumes, and complex carbohydrates, with a moderate consumption of fish, and the use of olive oil as the main source of fats. This eating pattern has been promoted worldwide as a model for healthy eating and has been reported to contribute to a favorable health status and to a better quality of life, as well as allowing an optimal intake of antioxidant vitamins, polyunsaturated fats and other beneficial nutrients for the prevention of chronic degenerative diseases. In terms of NAFLD prevention, the beneficial effects of such dietary habits can be explained through several mechanisms that can vary from an effective dietary approach for weight loss, to a model diet that is plentiful in some beneficial nutrients such as MUFA and vitamins, to the presence of olive oil as the main contributor of fats. Indeed, olive oil has been demonstrated to have several different beneficial effects on metabolic syndrome and NAFLD, by improving glucose and lipid metabolism and preventing atherogenesis. All these factors likely contribute, as a whole, in determining the preventive and therapeutic role of a Mediterranean diet on fatty liver disease.[29]

Consumption of selected dietary components is favorably associated with prevention of type 2 diabetes, but discordant results for some foods or single nutrients continue to appear. The study of complete dietary patterns represents the most adequate approach to assess the role of diet on the risk of diabetes. The term 'Mediterranean diet' essentially refers to a primarily plant-based dietary pattern whose greater consumption has been associated with higher survival for lower all-cause mortality. The diet was also associated with reduced coronary heart disease and stroke in women.[30]

FATS

Observational FATS

There is a strong degree of agreement between observational studies which show that a higher intake of SFAs, and a lower intake of polyunsaturated fatty acids (PUFAs),[31-33] is associated with NAFLD and NASH. In a NASH cohort, 7-day stool records revealed that persons with NASH consumed significantly higher proportions of SFAs and a lower percentage of PUFAs, although differences were also seen between their intake of cholesterol, fiber and anti-oxidant vitamins.[33] In a Japanese cohort the ratio of PUFAs to SFAs was also lower in persons with NASH and NAFLD compared to the general population.[32] These findings were replicated in a pediatric cohort in which SFA intake correlated proportionally to the degree of hepatic steatosis.[31] Furthermore, omega-3 fatty acid consumption was lower in pediatric NAFLD persons and this, along with insulin resistance, remained the most significant factor.[31]

Pathophysiology FATS

SFAs exert their effects on the liver through the promotion of insulin resistance and oxidative stress. They induce hepatic steatosis by increasing lipolysis as well as DNL, which occurs through the promotion of the transcription of peroxisome proliferator-activated receptor (PPAR) γ coactivator-1β and SREBP-1c.[34] SFAs also promote lipotoxicity through ceramides and diacylglycerides,[35] and can induce hepatocyte apoptosis and increase oxidative stress, which may encourage progression towards NASH.[36] Conversely, monounsaturated fatty acids (MUFAs) activate transcription factors PPARγ and PPARα, promoting safe fatty acid storage in adipose tissue and lipid detoxification via fatty acid oxidation, respectively.[37] PUFAs increase the transcription of PPARα, increasing lipid metabolism and mitochondrial oxidation, thereby reducing hepatic FFA concentrations.[38]

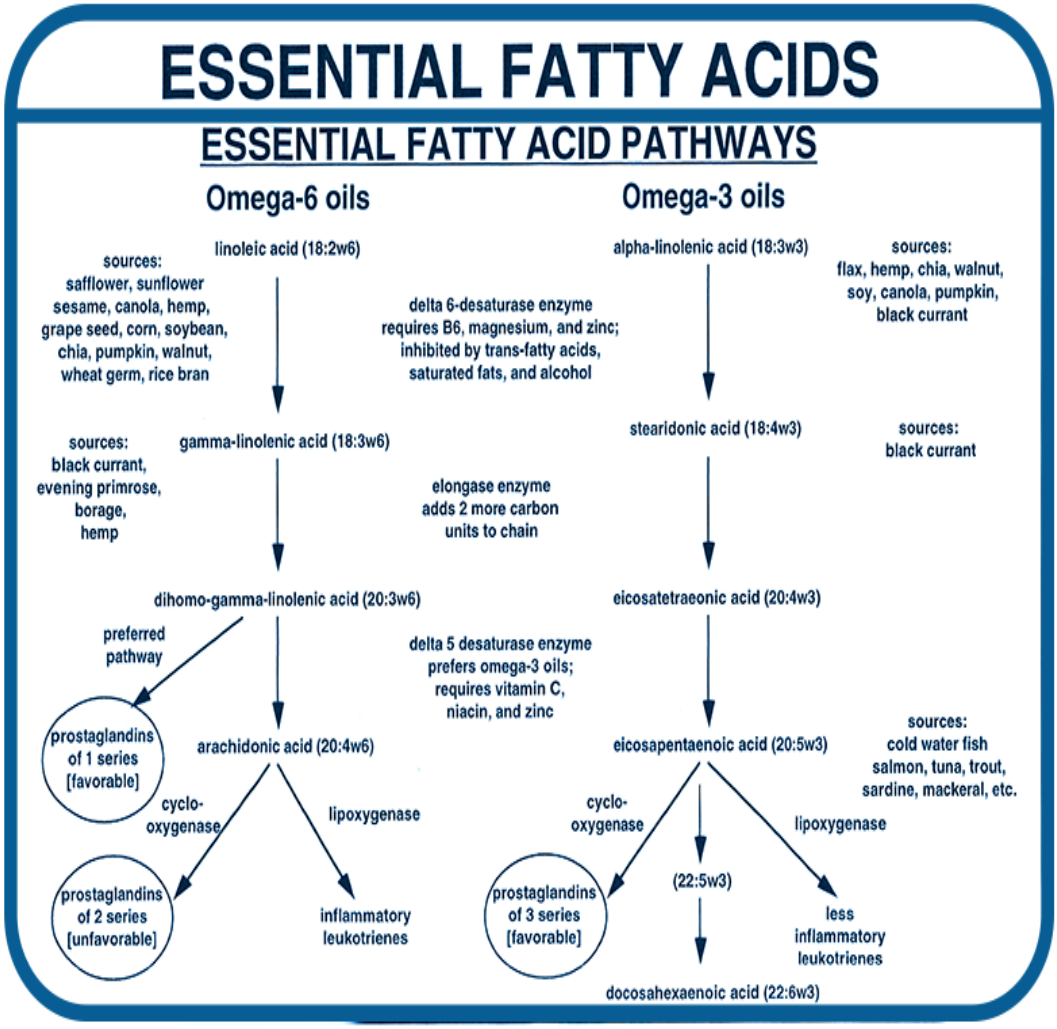
They also inhibit SREBP1c, reducing fatty acid synthesis.[39] Omega-3 fatty acids lower the hepatic triglyceride content by suppressing hepatic VLDL apolipoprotein B-100,[40] and inhibit inflammatory cells involved in NASH.[41]

Metabolism – fats

In dietary discussions fats are generally considered as a class. The implication is that it doesn't make much difference what specific fat is consumed. The typical analysis is about the caloric content and ignores the issue of specific metabolites. Health depends on consuming a variety of fats because they are converted to different things depending on their actual structure. That has significant consequences for health because you need the things that fats are made into by the liver. An easy illustration is with the omega 6 and 3 fatty acids that you must consume. Your body can make most of the kinds of fats that it needs but not these two.

Omega 6 metabolism compared to Omega 3

This is a simplified diagram of processes that the omega 6 and omega 3 fatty acids go through as they are manipulated by your body. All Fatty acids are involved in a wide array of chemical reactions which depend upon how they are actually made, that is how many carbons are in the chain and do they have kinks in them or not as just two important variables.[42]



Note, both fats are 18 carbon atoms long. The differences seem trivial as one has a kink at position 6 the other at position 3. That difference leads to different chemicals being produced as they are made into products that the body actually uses and the final products include different prostaglandins. You can see at the bottom that some products are more inflammatory, and some are less. Can you influence which kind your body makes? The interesting answer is yes. If you look at the center column where it says delta 5, that is the point where you have some influence.

It turns out that both essential fatty acids use the same enzyme at that step in their chemical processing. Delta 5 desaturase is a critical step for both processes. It is also useful that the enzyme prefers to work with the omega 3 oil. So, when you eat both omega 6 and omega 3 your body will tend to produce more prostaglandin 3 and other beneficial chemicals instead of prostaglandin 2 which is more inflammatory.

Why is that important? In our modern diet, omega 6 is found in the seed oils like cottonseed and soybean oils. Because those are very inexpensive, they have become a main source of calories in modern food manufacture. When you overload your body with omega 6 seed oils, which is everywhere today, you make it harder for your liver to combat inflammation. There are many sources of inflammatory materials so the more of them you can control with diet the easier it will be for your liver to function which contributes to liver health and what happens in the body.

If you understand that all fatty acids interact within your cells and because of differences in their length and specific structure there are chemical pathways that favor the various versions so there is more to the story of fats than just the fact that they are energy dense. Because of this complexity it is very difficult for researchers to consider effects at a fundamental level, so it is common to study broad ideas like total energy. Some studies make a distinction between saturated and unsaturated fats, but it is useful to keep in mind that there is usually more to the story even though the research, media and advertising speak to you about narrow ideas with great certainty.

In the broad category of classes of fat there is a major distinction between what we call saturated or unsaturated molecules. Fatty acids are long chains of carbon atoms strung together like beads on a string. If they all have hydrogen atoms attached to them, they are called saturated and if not they are unsaturated. This is important because if affects the kinds of chemical processes that particular molecule can easily engage in as well as the physical properties of the molecule in how flexible it is. Perhaps the best example is that omega 9, an 18-carbon unsaturated fatty acid, is more likely to be used for energy production than stearic acid, the saturated 18-carbon fatty acid, which is more likely to be deposited as fat. Omega 9 is oleic acid from olive oil and Stearic acid is tallow from beef.

Your body has tools for managing the wide range of fatty acids that you consume, but it is important to understand that some molecules present issues to be managed and others are supportive. How those balance out defines the workload that the cell is doing and ultimately have consequences for your long term health. We are focused here on fats, but the same issues arise

with a variety of things that are in our diet. We consume a wide array of fats, carbohydrates, and proteins that we need to live successfully, and it is the overall impact that determines health.

As an example of the kind of research that is being done today, the following table lists some of the studies focusing broadly on how those general molecular forms are processed by the body. These studies are examining the question of how saturated and unsaturated fat effect the body.

Trials - FATS

"The beneficial effects of PUFAs and MUFAs, and metabolically harmful effects of SFAs, are shown in Table 2"[5, 24, 77-79][3]. This data is from a report by Hydes et al[5]

Table 2.[5] Summary of randomized controlled trial data examining the influence of diets high in saturated fatty acids and poly- and mono-unsaturated fatty acids on hepatic steatosis

Study	Participant	Intervention	Result
Bozzetto et al.[34] (2012)	Adults with T2DM (n=45)	8 weeks diet, either: 1) high Carbohydrate / high-fiber / low-glycemic 2) high-MUFA diet; 3) high- glycemic patients consuming a high-carbohydrate, high-fiber, index diet plus physical activity; and low-glycemic index diet 4) high-MUFA diet plus physical activity	An isocaloric diet high in MUFA led to a reduction in liver fat, independent of index diet; weight loss and exercise
Bjermo et al.[43] (2012)	Obese adults (sagittal abdominal diameter >25 cm, or waist circumference >88 cm [women] or >102 cm [men]; n=67)	10 weeks isocaloric diet high in omega 6 PUFAs or SFAs (butter); no other changes to macronutrients	A modest increase in weight was seen, however this did not differ between groups. The SFA group had significant increases in liver fat (assessed using MRI), serum triglycerides, total and LDL cholesterol and insulin resistance compared to the group receiving PUFAs, in which all these markers improved.
Rosqvist et al.[12] (2014)	Young, normal weight adults (n=39)	750 extra kcal/day for 7 weeks from muffins high in SFAs vs. muffins high in PUFAs	The SFA group had greater increases in liver fat (P=0.033) and a 2-fold increase in VAT (P=0.035). The PUFA group had a 3-fold increase in lean tissue (P=0.015).
Errazuriz et al.[44] (2017)	Adults with pre-diabetes (n=43)	12 week isocaloric weight-maintaining diets: 1) high MUFAs (olive oil), 2) fiberrich, and 3) standard US food	Only the MUFA group demonstrated a significant decrease in liver fat fraction as determined by MRI (P<0.0003), in addition to improvements in hepatic and total insulin sensitivity.
Luukkonen et al.[7] (2018)	Overweight adults (mean BMI, 31±1 kg/m^2; n=38)	1,000 extra kcal/day for 3 weeks from either SFAs/unsaturated fat/simple sugars	Overeating 1,000 kcal/day of SFAs increased IHTG more than unsaturated fats (55% vs. 15%, P<0.05).

T2DM, type 2 diabetes mellitus; MUFA, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; SFAs, saturated fatty acids; MRI, magnetic resonance imaging; LDL, low-density lipoprotein; VAT, visceral adipose tissue; US, United States; BMI, body mass index; IHTG, intrahepatic triglyceride.

Two meta analyses have examined the effects of omega-3 supplementation on NAFLD. Both reported that omega-3 supplementation was beneficial in reducing liver fat, but did not impact liver biochemistry. [45, 46]

ENERGY AND CALORIC RESTRICTION

Observational ENERGY AND CALORIC RESTRICTION

The diabetes, obesity and NAFLD epidemics are products of dietary choices resulting in a significant rise in average energy intake and reduced energy expenditure. The increasing consumption of energy-dense foods and a sedentary lifestyle are fundamentally linked to obesity, increased inflammation and mitochondrial dysfunction. The imbalance is often driven by high quantities of saturated fatty acids (SFAs), refined carbohydrates (CHOS), sugar sweetened beverages (SSBs) and alcohol excess. Understanding the individual impact of these factors is a challenge.[5]

Pathophysiology ENERGY AND CALORIC RESTRICTION

A high-caloric diet leads to increasing fat tissue, which is a sentinel event in the development of NAFLD. Visceral adipose tissue (VAT) is a biologically active fat. Excess accumulation of VAT increases the production of FFAs through reduced insulin sensitivity, leading to increased fatty acid influx into the liver, DNL and insulin resistance. Enlargement of the liver (hypertrophy) and an accumulation of abnormal cells (hyperplasia} in the liver results in reduced oxygen levels (hypoxemia) and fat cell dysfunction.[47] This exacerbates insulin resistance and high fat levels in the blood, and creates a pro-inflammatory environment within the tissue. The secretion of cell signaling molecules and pro-inflammatory molecules (cytokines) from VAT create a state of systemic low-grade chronic inflammation which can promote the onset of both NAFLD and NASH.[48]

Trials - ENERGY AND CALORIC RESTRICTION

Weight loss is consistently identified as being central to the metabolic benefits that result from calorie restriction. A meta-analysis of therapeutic options for NAFLD, including lifestyle interventions, reported that weight loss of greater than 7% led to improved histological disease activity determined by the NASH Activity Score, although there was no impact on fibrosis.[49]

Guidelines currently recommend continuous energy restriction along with physical activity,[49] Several trials have looked at the effectiveness of intermittent fasting in the setting of NAFLD. Modified alternate-day calorie restriction was found to lead to reductions in BMI, liver enzymes, liver steatosis and liver stiffness compared to no intervention.[50] A larger trial comparing alternate-day and time-restricted feeding revealed that both diets led to significant short-term reductions in weight and improvements in blood lipid levels, although no changes were seen in fasting levels for insulin or liver stiffness.[51]

These studies lead to the advice for calorie restriction as a strategy with a 500–1,000 kcal daily deficit as an extremely effective lifestyle intervention for both the prevention of NAFLD and

histological improvement in persons with established disease. The goal of calorie reduction should be to achieve greater than 10% overall body weight loss. The challenge being that compliance and success are not commonly achieved by the average person.[5]

PROTEIN

Observational PROTEIN

The consumption of animal protein, specifically red and processed meat, is associated with higher all-cause, cardiovascular and cancer-related mortality compared to plant protein.[52, 53] In a large US study, red and processed meats were associated with nine causes of death, with the strongest correlation being for mortality from chronic liver disease.[54] Animal protein is positively associated with high fatty liver index scores, whereas plant protein is inversely related.[55] It is assumed that processed meats carry a greater risk burden due to an added chemical load but detailed studies are lacking.

Pathophysiology PROTEIN

Red and processed meats may lead to NAFLD, insulin resistance and T2D as a result of their high content of SFAs, cholesterol, iron, nitrates and nitrites, preservatives, advanced glycation end-products and branched chain amino acids (BCAAs).[56] Diets low in methionine (found predominantly in meat, fish and dairy products), can prevent the development of insulin resistance in animal models via activation of fibroblast growth factor 21 (FGF21) while activating hepatic FFA oxidation.[57, 58] Red and processed meats also contain high levels of phosphatidylcholine and L-carnitine, which are metabolized to trimethylamine (TMA) by gut microbiota. TMA is oxidized in the liver by hepatic flavin to form trimethylamine oxide (TMAO). TMAO promotes atherosclerosis via the up-regulation of multiple macrophage scavenger receptors,[59] and high TMAO levels correlate with increased incidence of major cardiovascular events.[60] Plasma TMAO levels correlate with the presence and severity of biopsy proven NAFLD in a large Chinese adult population.[61] Individuals eating a vegan diet have an altered intestinal microbiota composition compared to omnivores, with reduced capacity to produce TMAO.[62]

Trials - PROTEIN

RCTs are lacking to determine the impact of animal protein on the progression of NAFLD, it is reasonable, based upon known liver chemistry, for people with NAFLD to reduce their intake of red and processed meats in light of their increased cardiovascular risk.

There is a considerable body of research which supports a strategy of plant-based diets and limiting saturated fats but direct comparisons in the context of liver health are lacking and very difficult to perform. Similar arguments exist for diets such as KETO and there are many advocates for both of these very different approaches. It is worth considering that both KETO and vegan diets limit added sugars and simple carbs which is the core basis for the Liver Friendly Diet.

CARBOHYDRATES (CHOS)

Observational CARBOHYDRATES

Studies examining the association between carbohydrates (ChO) and NAFLD are unclear due to lack of differentiation between refined and unrefined CHOS. Low carb diets have been associated with higher all-cause and cardiovascular mortality. [63] In a small study, persons with NAFLD were found to have significantly higher intake of protein and CHOS, specifically mono- and disaccharides, compared to controls.[64] Protein and CHO intake correlated to higher ALT levels. High CHO intake has also been associated with higher aminotransferases and presence of the metabolic syndrome in a large Korean cohort.[65] There is confusion because the opposite was found in a Portuguese study comparing the diets of persons with NASH where lower CHO consumption was seen in persons with NASH.[66] In children, total CHO intake has also been shown to be significantly higher in obese children with NAFLD compared to those without. CHO intake has also been shown to increase in parallel to the degree of liver fat.[31]

The data on histologic impact of CHO consumption is limited. In a bariatric surgery study, higher CHO intake was significantly associated with inflammation, but not fibrosis, on liver biopsy.[66] In older adults with NAFLD, higher daily fructose consumption has been associated with fibrosis, hepatic inflammation and hepatocyte ballooning.[67]

Pathophysiology CARBOHYDRATES

CHOS induce DNL by activating the CHO responsive transcription factor and CHO response element binding protein.[68] Fructose is metabolized predominantly in the liver where it is converted into glyceraldehyde-3-phosphate and can be used for fatty acid production.[69] Diets high in fructose contribute to NAFLD by increasing DNL and reducing fatty acid oxidation.[70] Although data are lacking, unrefined CHOS are likely to be protective against NAFLD as a result of their lower glycemic index, higher fiber content, and their role in increasing production of short-chain fatty acids in the gut.[71]

Trials - CARBOHYDRATES

Meta-analysis of multiple RCT regarding CHOS showed that the overall conclusion was that a low CHO diet could reduce intrahepatic lipid content (IHLC) by over 10%. When low (less than 60 g/day) and high CHO (greater than 180 g/day) diets were compared, reduction in IHLC was comparable between both groups after 7% weight loss.[72] Furthermore, a direct comparison of hypocaloric diets (30% energy restricted) either low in CHO (and high in fat), or low in fat, revealed comparable decreases in body weight, visceral fat and IHLC.[73] Meta-analyses reported an association between a high fructose diet and NAFLD incidence and severity.[74]

In adolescent boys, those on a limited free sugar diet (less than 5% daily calories) for 8 weeks experienced a significant decrease in hepatic steatosis and aminotransferases compared to those

with no dietary intervention.[75] Over-feeding studies further highlight the association between sugar sweetened beverages and NAFLD.[76] Whole, unrefined CHOS are protective against cardiovascular disease, T2D, colorectal and breast cancer,[77] and are associated with decreased all-cause mortality,[78] however data in NAFLD is lacking.

FIBER

Observational FIBER

High fiber consumption is associated with a 15–30% decrease in all-cause and cardiovascular-related mortality, lower risk of heart disease, stroke, T2D and gastro-intestinal cancer.[77] Epidemiological studies suggest there may be an association between a low fiber diet and the development of NAFLD. Fiber consumption has also been shown to be significantly lower in obese children with moderate and severe hepatic steatosis, compared to obese children without NAFLD.[31] In a small study, liver enzymes normalized in 75% of NAFLD persons eating 10 g/day of soluble fiber for 3 months.[79] The study was limited not only by lack of a control group, but also reduction in BMI, waist circumference, insulin resistance index and cholesterol levels in two thirds of persons.[5] This is an illustration of the variety of confounders that make diet studies difficult.

Pathophysiology FIBER

The majority of studies looking at the benefits of fiber on cardiovascular risk factors have focused on soluble fiber. Soluble fiber is thought to be protective against NAFLD by reducing serum low-density lipoprotein (LDL)-cholesterol levels.[80] The mechanism for this is unclear, although it has been proposed that soluble fiber may bind to bile acids or cholesterol, lowering the cholesterol concentration in liver cells (hepatocytes), leading to up-regulation of LDL receptors and clearance of LDL cholesterol.[81] Soluble fiber can also slow the rate at which CHOS are absorbed into the circulation reducing high blood sugar spikes. High fiber foods have a low glycemic index leading to improved glucose tolerance.[82]

Trials - FIBER

In research areas other than liver disease, dietary fibers are known to have a protective effect against certain gastrointestinal diseases, constipation, hemorrhoids, colon cancer, gastroesophageal reflux disease, duodenal ulcer, diverticulitis, obesity, diabetes, stroke, hypertension and cardiovascular diseases.[83]

RCTs studying the effect of fiber intake in isolation on NAFLD are lacking, as this usually forms part of a wider dietary intervention. In one study, individuals with metabolic syndrome were randomized to two energy-restricted diets for 6 months.[84] Participants who consumed higher levels of fiber from fruit experienced improvements in their fatty liver index, hepatic steatosis index, NAFLD liver fat score and liver enzymes, supporting the idea favoring consumption of fiber in the context of energy restriction. In a small, crossover trial, persons with NASH received a dietary

fiber, or placebo for 8 weeks. The fiber led to a significant reduction in insulin levels, as well as ALT and AST independent of a significant effect on plasma lipids.[85]

DIETS – General discussion

Mediterranean

One of the best-studied diets for cardiovascular health is the Mediterranean diet. This consists of fish, monounsaturated fats from olive oil, fruits, vegetables, whole grains, legumes/nuts, and moderate alcohol consumption. The Mediterranean diet has been shown to reduce the burden, or even prevent the development, of cardiovascular disease, breast cancer, depression, colorectal cancer, diabetes, obesity, asthma, erectile dysfunction, and cognitive decline. This diet is also known to improve surrogates of cardiovascular disease, such as waist-to-hip ratio, lipids, and markers of inflammation, as well as primary cardiovascular disease outcomes such as death and events in both observational and randomized controlled trial data.[86]

The Mediterranean diet can also decrease inflammation and promote a healthy digestive tract. Microbes in the gastrointestinal tract are necessary for proper digestive function and may benefit from a diet rich in plant-based foods.[3] Components in western diets may have undesirable effects on the pathogenesis of disorders such as inflammatory bowel diseases, cardiovascular disease, and type 2 diabetes. Components associated with unhealthy fats including phosphatidylcholine, and L-carnitine have been implicated in promoting inflammation and atherosclerosis. The by-products of fatty acid degradation induce these undesirable effects in the gastrointestinal tract and throughout the body.[87]

Type 2 diabetes (T2D) is a growing national health problem affecting 35% of adults older than 20 years of age in the United States. Recently, diabetes has been categorized as an inflammatory disease, sharing many of the adverse outcomes as those reported from cardiovascular disease. Medical nutrition therapy is recommended for the treatment of diabetes; however, these recommendations have not been updated to target the inflammatory component, which can be affected by diet and lifestyle. The Mediterranean and DASH diets were associated with lower inflammatory markers. The Mediterranean diet demonstrated the most clinically significant reduction in glycosylated hemoglobin (HbA_{1c}). Information on best dietary guidelines for inflammation and glycemic control in individuals with T2D is lacking.[88]

While RCT data is sparse with regard to NAFLD/NASH specifically, research suggests that the Mediterranean diet (rich in plant-based foods, legumes and unsaturated fats) should prove ideal for persons with NAFLD as a result of its effectiveness as a form of primary prevention for components of the metabolic syndrome, and ability to reduce insulin resistance, liver fat and inflammation.[89] A Mediterranean diet compared to a low-fat diet showed similar reductions in hepatic steatosis over 12 weeks with similar weight loss in both groups. The Mediterranean group, however, saw improvements in cholesterol, triglycerides and hemoglobin A1C.[90] Obese individuals with diabetes asked to follow a modified Mediterranean diet for 12 months were found to display lower

levels of ALT compared to participants allocated to the American Diabetes Association diet and a low glycemic index diet.[25] The Mediterranean diet is recommended by EASL for the management of NAFLD.[91]

Vegetarian - Vegan

Vegetarians and vegans have a lower prevalence of overweight and obesity and a lower risk of heart disease compared with non-vegetarians from a similar background, whereas the data are equivocal for stroke. For cancer, there is some evidence that the risk for all cancer sites combined is slightly lower in vegetarians than in non-vegetarians, but findings for individual cancer sites are inconclusive. Vegetarians have also been found to have lower risks for diabetes, diverticular disease and eye cataract. Overall mortality is similar for vegetarians and comparable non-vegetarians, but vegetarian groups compare favorably with the general population. The long-term health of vegetarians appears to be generally good, and for some diseases and medical conditions it may be better than that of comparable omnivores though more research is needed.[92]

DASH

The DASH (Dietary Approaches to Stop Hypertension) diet is a low-glycemic, low energy, fiber dense diet characterized by high intake of fruits and vegetables, whole grains, and low fat dairy products, with limited SFAs. Studies regarding the DASH diet are limited, however, the high fiber and antioxidant content, and low saturated fat and refined CHOS content, is likely to be beneficial for NAFLD.[93]

KETO, Atkins and Other Low Carb Diets

Nonalcoholic steatohepatitis (NASH) is strongly associated with obesity. A weight loss of ≥10% is necessary to improve NASH severity, but this goal has rarely been achieved in published studies using different diet protocols. The effect of a ketogenic, hypocaloric, commercial diet ("Ideal Protein," IP) on body weight, metabolic markers, and liver tests has been shown to produce striking weight loss and significant improvements in metabolic parameters and liver tests, suggesting that this approach carries promise for the dietary management of patients with NASH.[94] Longer term effects on the microbiome and other potential health impacts require additional study. The Keto diet is inconsistent with the Liver Friendly diet long term because of the high saturated fat and protein content but it is effective for short term weight loss though many find it hard to maintain. Anyone considering it in the context of NAFLD/NASH should discuss it thoroughly with their physician.

BEVERAGES

Sugar Sweetened Beverages

Consumption of dietary fructose has been shown to be significantly higher among NAFLD persons compared to controls.[95, 96] In the Framingham Heart Study, higher consumption of SSBs incrementally increased the odds ratio for NAFLD even after adjustment for BMI, energy intake, dietary fiber, fat, protein, and diet soda.[97] SSB consumption was also positively associated with ALT levels in this group. After controlling for dietary composition and physical activity, SSB consumption has been shown to be an independent variable to predict NAFLD.[98]

Alcohol

Study has shown that steatosis is present in nearly 95% of obese persons who drink more than 60 g of alcohol per day, however obesity plays the over-arching role.[99] There is, however, strong evidence that persons drinking more than 2 drinks/day for women and more than 3 drinks/day for men with NAFLD are at significantly increased risk of developing advanced liver fibrosis.[100] Even mild to moderate drinking has been found to increase the risk of steatohepatitis, fibrosis, decompensated liver disease, mortality and liver cancer among individuals with obesity and diabetes.[101-106] Abstinence has been advocated for persons with NASH cirrhosis in order to reduce the risk for decompensation and hepatocellular carcinoma (HCC).[107]

Coffee

Large systematic reviews have shown that coffee leads to a relative risk reduction of cirrhosis and liver-related mortality secondary to all causes.[108, 109] Meta-analysis has shown that more than 3 cups per day reducing the incidence of NAFLD significantly.[110] Several constituents found within coffee have been suggested as being mechanistic due to their favorable effects on glucose metabolism.[111]

Green Tea

The health benefits of green tea for a wide variety of ailments, including different types of cancer, heart disease, and liver disease, have been reported. Many of these beneficial effects of green tea are related to its catechin content. There are human studies on using green tea catechins to treat metabolic syndrome, such as obesity, type II diabetes, and cardiovascular risk factors.[112]

Green tea consumption has also been associated with increased bone mineral density, and it has been identified as an independent factor protecting against the risk of hip fractures; this effect was considered independent of smoking status, hormone replacement therapy, coffee drinking, and the addition of milk to tea showed positive effects of green tea extracts and GTPs on the proliferation and activity of bone cells.[113] The proliferation of hepatic stellate cells is closely

related to the progression of liver fibrosis in chronic liver diseases, and EGCG has a potential inhibitory effect on the proliferation of these cells. [114]

Dairy products

There is some skepticism about health effects of dairy products in the public, which is reflected in an increasing intake of plant-based drinks, for example, from soy, rice, almond, or oat. Intake of milk and dairy products was associated with a neutral or reduced risk of type 2 diabetes and a reduced risk of cardiovascular disease, particularly stroke. The evidence suggests a beneficial effect of milk and dairy intake on bone mineral density but no association with risk of bone fracture. Among cancers, milk and dairy intake was inversely associated with colorectal cancer, bladder cancer, gastric cancer, and breast cancer, and not associated with risk of pancreatic cancer, ovarian cancer, or lung cancer. [115] The use of low and non-fat dairy products is believed to be beneficial and are a normal part of the Liver Friendly Diet. It should be noted that nutritionally, cow's milk and plant-based drinks are completely different foods, and an evidence-based conclusion on the health value of the plant-based drinks has been demonstrated as well.[116]

Probiotics

Probiotic therapies can reduce liver aminotransferases, total-cholesterol, TNF-α, and improve insulin resistance in NAFLD patients. Modulation of the gut microbiota represents a new treatment for NAFLD.[117] Probiotics treatment may reduce liver fat and AST level in NASH patients but larger trials are needed. [118]

SOY

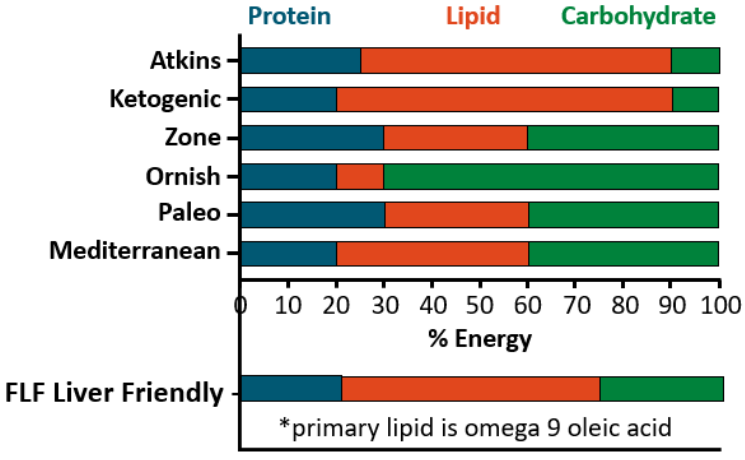
Soy is also thought to be helpful in NAFLD by inhibiting SREBP1c and activating PPARα, reducing lipid deposition and increasing antioxidant capacity. A study comparing persons eating a low calorie diet to a low calorie, soy-containing diet, reported that individuals eating the soy-containing diet had significantly greater improvements in liver tests and serum insulin levels.[119]

CONCLUSION

The Fatty Liver Foundation recommends a diet high in oleic acid (omega 9) unsaturated fat (30%), primarily from extra virgin oil, low is saturated and trans fats (7%), with omega 3 and 6 approximately equal (8% each). Protein is about 20% of calories and carbohydrates are primarily in the form of fruits, non-starchy vegetables, and whole grains (27%). Simple carbs, such as sugars and refined grains, are minimized as is alcohol. The goal for salt intake is about 70% of the USDA recommendation. Processed foods and red and processed meats are avoided.

Overall, the current data is supportive of diets low in SFAs, red and processed meats, and refined carbohydrates with increased use of poly and unsaturated fats for NAFLD. Diets focusing specifically on reducing carbohydrate or fat intake miss out on the benefits of whole grains, fiber, and unsaturated fats, which do not need to be minimized in the diet. These diets are also not sustainable for many. Diets that incorporate these recommendations include plant-based diets such as the DASH, Mediterranean, vegetarian, and vegan.

The use of extra virgin olive oil as a source of omega 9 unsaturated fat should be emphasized. A diet enriched in Extra Virgin Olive Oil and Omega 3 fatty acids will be, at a minimum, not directly harmful to the liver and is likely to provide a benefit. This informs the dietary advice provided to members of the Fatty Liver Foundation. Absent definitive research, which inhibits professional liver societies from making specific recommendations, it is still necessary to devise a dietary strategy which is likely to be beneficial to the general public health.



Weight loss resulting from consumption of a diet lower in carbohydrates and higher in fat may also be beneficial for older adults with obesity by depleting adipose tissue depots most strongly implicated in poor metabolic and functional outcomes and by improving insulin sensitivity and the lipid profile.[120] The Liver Friendly Diet is fundamentally a whole body friendly diet as the goal is

to provide all organs with those things they need for health without overloading any of the processes required for health.

It should be noted that we don't know enough to be able to create a diet that is truly efficient and serves our health needs unambiguously. Based upon the state of current research, this is the best approximation we know how to make that is specifically supportive of liver health.

Please consult with your doctor about your diet as broad discussions like this cannot substitute for the detailed understanding of your individual situation. Everyone is different and no strategy seeking to inform society broadly can apply to individual variations in genetics or circumstances.

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