MERCOLA
Take Control of Your Health

Liver Damage Is a Growing Epidemic

Analysis by Dr. Joseph Mercola ✔ Fact Checked

STORY AT-A-GLANCE

- Between 2000 and 2016, the annual death toll from liver cancer in the U.S. rose by 43% for men and 40% for women. Globally, hepatocellular carcinoma is the third leading cause of cancer death
- Other liver-related diseases such as cirrhosis and nonalcoholic fatty liver disease (NAFLD) are also becoming more prevalent, both of which raise your risk of liver cancer
- Between 2001 and 2013, diagnosed cirrhosis cases nearly doubled; deaths from cirrhosis increased by 65% between 1999 and 2016. The greatest increase was among those between the ages of 25 and 34, where alcoholic cirrhosis has become rampant
- Alcohol-induced cirrhosis and NAFLD can be reversed in their early stages by quitting drinking and cutting out processed fructose, respectively
- Folate, milk thistle, NAC, coffee and broccoli all help promote healthy liver function

This article was previously published August 1, 2018, and has been updated with new information.

According to the American Cancer Society (ACS),[1] liver cancer affects an estimated 41,260 Americans each year, and prevalence is rising.[2] Between 2000 and 2016, the annual death toll from liver cancer rose by 43% for men and 40% for women,[3] killing more than 11,000 people in 2016.[4]

In January 2022, the ACS estimates that 30,520 people will die from liver cancer in this year alone, adding, “Liver cancer incidence rates have more than tripled since 1980, while the death rates have more than doubled during this time.”

The five-year survival rate for localized liver cancer is 34 percent,[5] while regional cancer that has spread to other organs and distant liver cancer have survival rates of just 12 percent and 3 percent respectively.

Globally, the liver cancer hepatocellular carcinoma (HCC) is the third leading cause of cancer death[6] due to the high prevalence and difficulty of treatment. Researchers warn that by 2030, the global rate of liver cancer will double, affecting upward of 1.2 million.[7]

Other liver-related diseases such as cirrhosis, nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH)[8] are also becoming more prevalent. Between 2001 and 2013, the number of diagnosed cirrhosis cases nearly doubled,[9] and deaths from cirrhosis increased by 65 percent between 1999 and 2016.[10] The greatest increase (10.5 percent) was among those between the ages of 25 and 34, where alcoholic cirrhosis has become rampant.[11,12]

As a precursor for cancer, cirrhosis causes more than 1 million deaths a year worldwide,[13] with the incidence of NASH more than doubling from 1990 to 2017.

Excess Alcohol Consumption Drives Risk of Liver Damage

According to researchers, the rise in cirrhosis mortality is entirely driven by excess alcohol consumption by young adults. While, historically, alcohol-related liver cirrhosis has been regarded as a condition that develops after two or three decades of heavy drinking, these newer statistics reveal it doesn't have to take that long at all, as it's now occurring in (and killing) 20- and 30-year-olds.

In the 25 to 34 age group, death from alcohol-related liver disease nearly tripled between 1999 and 2016. This increase parallels statistics[14] showing a rise in binge drinking between 2002 and 2012. It also correlates with the global financial crisis in 2008, after which more people began dying from cirrhosis. Researchers believe financial

worries and unemployment may be significant contributing factors, causing more people to drink more heavily.

Cirrhosis (irreversible scarring of your liver) can also be caused by obesity, NAFLD and hepatitis, and can in turn lead to fatal liver failure and/or liver cancer. Men are particularly at risk, in large part because they're five times more likely to develop NAFLD than women.

Lifestyle factors such as diet, exercise, weight, smoking and alcohol consumption also play important roles in exacerbating (as well as reducing) your chances of developing some form of liver disease.

People at increased risk also include those who have an autoimmune disease, chronic liver inflammation and those whose livers have been damaged due to bouts of hepatitis B or C. The good news is that alcohol-related liver cirrhosis can be reversed if caught early enough — and provided you quit drinking.

Excess Sugar Consumption Drives Rising NAFLD Rates

While alcohol-related cirrhosis is driving up mortality rates, rising prevalence of NAFLD is contributing to the overall burden of liver-related diseases. In the case of NAFLD, the fatty liver occurs in the absence of significant alcohol consumption, and is driven instead by excess sugar, which is why this condition is now found even in young children.

NAFLD often has no symptoms, although it may cause fatigue, jaundice, swelling in the legs and abdomen, mental confusion and more. If left untreated, it can cause your liver to swell, called nonalcoholic steatohepatitis (NASH), and can lead to liver cancer or liver failure. As with alcohol-related cirrhosis, however, NAFLD can be reversed in its early stages by healthy eating and exercising.

Most importantly, you need to eliminate processed fructose and other added sugars from your diet. Fructose actually affects your liver in ways that are very similar to alcohol. Unlike glucose, which can be used by virtually every cell in your body, fructose

can only be metabolized by your liver, as your liver is the only organ that has the transporter for it.

Since all fructose gets shuttled to your liver, if you consume high amounts of it, fructose ends up taxing and damaging your liver in the same way alcohol and other toxins do. The way your liver metabolizes fructose is also very similar to that of alcohol,[15] as both serve as substrates for converting carbohydrates into fat, which promotes insulin resistance, dyslipidemia (abnormal fat levels in the bloodstream) and fatty liver.

Fructose also undergoes the Maillard reaction with proteins, leading to the formation of superoxide free radicals that can result in liver inflammation similar to acetaldehyde, an intermediary metabolite of ethanol. According to Dr. Robert Lustig, a neuroendocrinologist in the division of endocrinology at the University of California, fructose is a "chronic, dose-dependent liver toxin."

Excess Glucose Converts to Fructose and Decimates Your NAD+

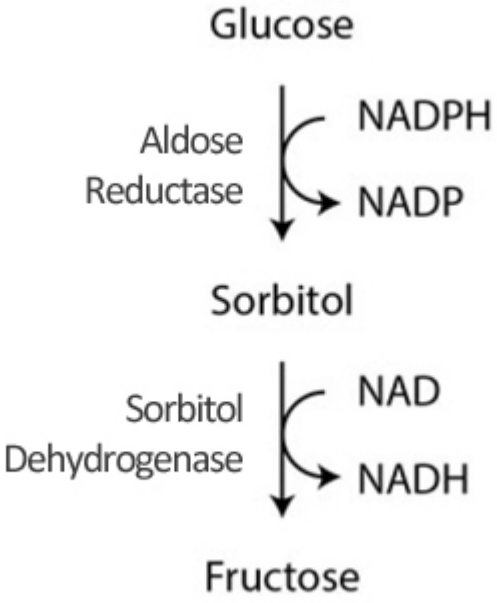
A few years ago I read an excellent review[16] on NAD that helped me understand the basic biochemistry far better, and it makes perfect sense. I learned that excess fructose in processed foods isn't the only problem, as excess glucose is ultimately converted to fructose by your body in an effort to metabolize glucose for energy. Let me explain it to you.

When your body is exposed to chronic glucose excess, the first enzyme in breaking down glucose is hexokinase, and this enzyme becomes saturated and can't break down any more glucose. Once this occurs, glucose will then be metabolized through the polyol pathway, in which glucose is metabolized to sorbitol by aldose reductase, and sorbitol is subsequently metabolized to fructose by sorbitol dehydrogenase (see figure below).

It is estimated when you are healthy, only about 3% of glucose goes through the pathway below, but at least 30 percent of glucose flows through this pathway in chronic hyperglycemia,[17] creating a vicious cycle of excess fructose.

This metabolic catastrophe is the net redox result of the trading of one molecule of NADPH for one molecule of NADH. This is precisely what you don't want to happen, as NADPH is used as a reductive reservoir for your antioxidants and is necessary to make your steroid hormones and fats. When you have low levels you are in deep trouble.

Complicating it further, you increase NADH and worsen your NAD+/NADH ratio. As fuel supply outstrips metabolic demand, mitochondrial and cytoplasmic NAD/NADH ratios fall. The ensuing mitochondrial membrane hyperpolarization perpetuates electron leakage and excessive oxidative stress.



Fortunately, the good news is that there is a simple inexpensive solution that should radically improve this metabolic catastrophe. The first, of course, is to clean up your diet as we have previously discussed many times, so your body can burn fat for fuel. But you can also take NAD precursors like simple nontimed-release niacin.

That should help increase the NAD+/NADH ratio and NADPH levels. As noted in one recent paper,[18] "Oral administration of nicotinamide riboside, a natural NAD+ precursor, completely corrected these NAFLD phenotypes induced by NAD+ deficiency."

I would start non-timed release niacin at 25 to 50 milligrams a few times a day, as any dose higher will likely cause a harmless but relatively annoying flushing sensation. It

would also be helpful to reduce your exposure to electromagnetic fields, as that also consumes NAD+ through PARP hyperactivation and will worsen the metabolic condition.

Low-Level Chemical Exposures Linked to Liver Damage

While there's no data on this, it's possible that alcohol-induced cirrhosis is now occurring sooner as a result of liver damage caused by chemical exposures. Researchers have shown that even small amounts of chemicals from food, pharmaceuticals and personal care products can in fact cause liver damage.

One such experiment[19] was designed to evaluate the effects of chemical combinations at low doses from environmental sources such as food, pharmaceuticals and personal care products.[20]

Using four groups of Sprague-Dawley rats, the researchers administered a mix of chemicals found in everyday products in their drinking water at varying doses for a period of six months. The control group received chemical-free water.

Of the three treatment groups, the low-dose group received 25% of the European Union (EU) acceptable daily intake for the chemicals in question, the medium-dose group received exactly the acceptable daily intake defined by the EU, while the high-dose group received five times the acceptable daily intake.[21]

After six months, body weight and biochemistry markers were evaluated, revealing the animals' weight increased more than 10% in all male groups, compared to controls.[22] Modest increases were found in females given medium and high doses of the chemicals.

They also discovered adverse liver effects — especially at the low-dose level and primarily in the males. Overall, the results suggest exposure to low doses may induce liver damage as a result of the combination of different toxic mechanisms, and support previous research showing that chemical cocktails, even at low levels,[23] can damage liver function[24] and trigger cancer.[25]

Roundup Damages Liver at Ultralow Doses

Roundup, the most heavily-used weed killer in the world, has also been linked to liver damage. Disturbingly, urine levels of glyphosate have skyrocketed in the past couple of decades, suggesting widespread, chronic exposure, most likely from food. Between 1993 and 2016, levels of the chemical in human urine increased 1,200 percent.[26] Food testing also reveals that many foods sold in the U.S. are contaminated with glyphosate.[27]

This is of significant concern, as research suggests Roundup can cause significant liver damage even at ultralow doses. The study,[28] published in the journal Scientific Reports, looked at the effects of glyphosate exposures of 4 nanograms per kilogram of body weight per day, which is 75,000 and 437,500 times below EU and U.S. permitted levels, respectively.

After a two-year period, female rats showed signs of liver damage, specifically NAFLD and progression to nonalcoholic steatohepatosis (NASH). Study author Michael Antoniou, Ph.D., told Sustainable Pulse:[29]

> *"The findings of our study are very worrying as they demonstrate for the first time a causative link between an environmentally relevant level of Roundup consumption over the long-term and a serious disease — namely nonalcoholic fatty liver disease. Our results also suggest that regulators should reconsider the safety evaluation of glyphosate-based herbicides."*

Milk Thistle Helps Prevent Liver Damage

Milk thistle is an herb that has been used for thousands of years to support liver, kidney and gallbladder health. In modern times, silymarin has been used to treat alcoholic liver disease, acute and chronic viral hepatitis and toxin-induced liver diseases.

The active ingredient, a flavonoid called silymarin, is thought to be responsible for the beneficial effects attributed to milk thistle, including liver protection, antioxidant,

antiviral and anti-inflammatory properties. In your liver, silymarin works as an antifibrotic, thereby preventing tissue scarring, and blocks toxins by inhibiting the binding of toxins to liver cell membrane receptors. Silymarin also protects your liver and promotes healthy liver function by:

- Suppressing cellular inflammation[30]
- Inhibiting the mammalian target of rapamycin (mTOR), a pathway that, when overactivated, increases your risk of cancer[31]
- Activating AMPK (activated AMP-activated protein kinase),[32] an enzyme inside your cells. AMPK is sometimes referred to as a "metabolic master switch," as it plays an important role in regulating metabolism and energy homeostasis.[33] AMPK produces many of the same benefits as you would get from exercise and weight loss, both of which benefit your liver health
- Reducing liver injury caused by a number of drugs and environmental toxins, including acetaminophen, chemotherapy, psychotropic drugs and alcohol
- Increasing glutathione, a powerful antioxidant that plays a role in the detoxification of heavy metals and other harmful substances

N-acetylcysteine Supplement Supports Your Liver Health

Another powerful liver protectant is N-acetylcysteine (NAC), a precursor needed for glutathione biosynthesis. In fact, research suggests NAC may be a better alternative for supporting liver health in those with hepatitis C and other chronic liver diseases than the antioxidant resveratrol.[34]

Alcohol and acetaminophen are two common compounds metabolized through the liver that are associated with liver damage. NAC supplementation has been effective in minimizing damage associated with alcohol consumption when taken prior to alcohol ingestion.[35]

NAC is also used as an antidote for acetaminophen toxicity, which causes liver damage by depleting glutathione.[36] Research published in Hepatitis Monthly[37] has also shown

NAC supplementation helps improve liver function in patients with NASH.

Folate Deficiency Worsens Severity of NASH

Increasing your intake of folate can also help protect your liver function. In a study[38] involving 83 patients with NASH, researchers found levels of folate and vitamin B12 were inversely related to the development of fibrosis or the formation of scar tissue. Past research has identified an association between low levels of vitamins and chronic liver disease, but this is the first to find an association between folate and vitamin B12 level to NASH severity.

Studies have also shown folate deficiency can increase your risk for liver cancer.[39,40] In one, which involved hepatitis B-positive patients (who are at higher risk for liver damage), higher folate levels were associated with a 67 percent lower risk of liver cancer.[41]

According to the authors, increased folate in humans appear to be inversely associated with the development of liver damage and hepatocarcinoma, and that folate can offer the liver some degree of protection against damage. Folate may also mitigate against pesticide-related damage, including autism.

Your body stores approximately 10 to 30 milligrams of folate at a time, nearly 50 percent of which is in your liver. Folate is the natural form of vitamin B9 found in foods and once referred to as folacin. The word was derived from the Latin "folium," meaning leaf. Green leafy vegetables such as spinach are abundant sources of folate, as are asparagus, broccoli, Brussels sprouts and spinach.[42] Broccoli is perhaps ideal, as research[43] has confirmed it helps protect against NAFLD.

Avoid folic acid supplements however. While readily absorbed, this synthetic form is not converted in the intestines like folate is. Instead, it is converted in your liver. This means folic acid can reach saturation quicker, which may result in overexposure if you're taking supplements.

Coffee May Cut Risk of Liver Cancer

Last but not least, if you're a coffee drinker, you may be relieved to find out that coffee appears to have a protective effect against HCC, a serious form of liver cancer and the third-most prevalent cause of death from cancer in the world. Drinking a single cup of coffee every day cuts your risk of HCC by one-fifth.[44,45]

If you drink more than that in a day, your risk for liver cancer is even lower. Two cups of coffee a day cut the risk by 35%, and five cups cut the risk in half. That said, excessive coffee consumption can have certain adverse effects. As noted by lead author Dr. Oliver Kennedy from the U.K.'s University of Southampton:[46]

> *"We're not suggesting that everyone should start drinking five cups of coffee a day though. There needs to be more investigation into the potential harms of high coffee-caffeine intake, and there is evidence it should be avoided in certain groups, such as pregnant women."*

To optimize your health benefits from coffee, make sure it's organic, and drink it black, without milk or sugar. A far better alternative would be "bulletproof coffee," where you add butter or MCT oil to the coffee instead of sweeteners.

Sources and References

- [1] American Cancer Society, January 2021
- [2] New York Times July 18, 2018
- [3] CDC.gov NCHS Data Brief No. 314, July 2018
- [4, 10] BMJ 2018;362:k2817
- [5] American Cancer Society. Liver Cancer Survival Rates. January 29, 2021
- [6] American Cancer Society. A Cancer Journal for Clinicians. February 4, 2021
- [7] The University of Southhampton 2017
- [8, 13] Scientific Reports. 11, Article number: 5195 (2021). March 4, 2021
- [9] Gastroenterology 2015 Nov;149(6):1471-1482.e5; quiz e17-8
- [11] NPR July 18, 2018
- [12] Washington Post July 18, 2018
- [14] American Journal of Public Health 2015 Jun;105(6):1120-7
- [15] Journal of the American Dietetic Association, September 2010; 110(9): 1307-1321
- [16] Pyridine Dinucleotides from Molecules to Man 2018; 28(3)

- [17] Diabetes 1984 Feb;33(2):196-9
- [18] Antioxid Redox Signal. 2018 Feb 7
- [19, 21] Food and Chemical Toxicology, 2018;115:470
- [20, 22] GMWatch, June 7, 2018
- [23] Annals of Occupational and Environmental Medicine, 2013;25:5
- [24] World Journal of Gastroenterology, 2012; 18(22):2756
- [25] Carcinogenesis, 2015;36(1): 2254
- [26] JAMA. 2017;318(16):1610-1611
- [27] EWG. EWG's 2021 Shopper's Guide to Pesticides in Produce. March 17, 2021
- [28] Scientific Reports January 9, 2017; 7 article number 39328
- [29] Sustainable Pulse January 9, 2016
- [30] Journal of Natural Products, 2015; 78(8):1990
- [31] Methods in Molecular Biology, 2012;821:1
- [32] National Center for Complementary and Integrative Health, Study of Milk Thistle's Effects Highlights a Two-Phase Process
- [33] American Journal of Physiology, 1999;277(1 Pt 1):E1
- [34] World Journal of Gastroenterology, 2010; 16(15): 1937
- [35] Indian Journal of Clinical Biochemistry 1994; 9(64)
- [36] World Health Organization, Second Meeting of the Subcommittee of the Expert Committee on the Selection and Use of Essential Medicines
- [37] Hepatitis Monthly, 2010; 10(1):12
- [38] Nutrients, 2018;10(4):440
- [39] Cancer, Epidemiology, Biomarkers and Prevention, 2007;16(6):1279
- [40, 41] Nutraingredients, July 19, 2008
- [42] Harvard T.H. Chan School of Public Health. Folate — Vitamin B9
- [43] J Nutr March 2016;146(3):542-50
- [44] BMJ Open 2017; 7(5)
- [45] Medical News Today May 30, 2017
- [46] CBS Philly May 30, 2017