Nonalcoholic fatty liver disease

A growing health concern

You’ve always limited your alcohol consumption to an occasional glass of wine or cocktail. But after a routine blood test at your last checkup showed elevated levels of certain liver enzymes, your doctor is concerned that you may have nonalcoholic fatty liver disease (NAFLD).

NAFLD — a condition in which excess fat accumulates in the liver of people who drink little or no alcohol — has become one of the most common liver diseases in the U.S. Currently, it’s estimated that the disorder affects up to 20 percent of American adults. Researchers believe this is associated with rising rates of obesity.

A buildup of fat

Still, NAFLD often goes unnoticed because it usually causes no signs or symptoms. In its simplest form, it also tends to be free of complications. However, a buildup of fat in the liver can result in inflammation and scarring (fibrosis). This more serious form of NAFLD — called nonalcoholic steatohepatitis, or NASH — can cause severe liver damage and eventually lead to liver failure or liver cancer in a small percentage of people.

Your liver performs many tasks, including processing what you eat and...
drink into energy and nutrients and filtering harmful substances from your blood.

With NAFLD, fat builds up in liver tissue. Some people may experience fatigue, weight loss and pain in the upper right abdomen. However, these warning signs are rare, especially in the early stages.

Fat in the liver sometimes causes inflammation. This can cause scars to develop. Over time, these scars can harden your liver and impair its ability to function properly — a condition known as cirrhosis.

Only about 5 percent of people with NAFLD will develop cirrhosis, liver failure or liver cancer. However, the number of people with either NAFLD or NASH is on the rise. NASH is the third leading cause of liver transplants in the U.S. adults, and is becoming a more common reason for liver transplants in the U.S.

**Contributing factors**

A number of diseases and conditions can increase your risk of fatty liver disease. They include:

- **Obesity** — An excess amount of body fat may contribute to fat accumulation in the liver. Experts now estimate that about two-thirds of obese adults and half of obese children may have fatty livers.

- **High blood cholesterol** — Many people with NAFLD also have increased levels of fat (lipids) in their blood. These fats include low-density lipoprotein (LDL) cholesterol and triglycerides.

- **Type 2 diabetes** — With type 2 diabetes, your body either resists the effects of insulin — a hormone that regulates the movement of sugar into your cells — or doesn’t produce enough insulin to maintain a normal glucose level. As a result, glucose can build up in your blood and cause damage to your liver and other major organs.

Other risk factors for NAFLD include malnutrition and rapid weight loss. Certain medications, such as steroids, and exposure to some toxins and chemicals also may contribute to fatty liver disease.

If you have NAFLD, it may not be discovered until a routine blood test shows an elevation in certain liver enzymes. Additional blood tests may then be ordered to rule out other causes of liver disease, such as viral hepatitis.

To confirm the presence of fat in your liver, doctors often perform an imaging procedure — such as ultrasound, computerized tomography (CT) or magnetic resonance imaging (MRI). Doctors also may recommend a liver biopsy to examine a sample of tissue for signs of inflammation and scarring. Another, less invasive option that might be available is magnetic resonance elastography, a new type of imaging technology that uses sound waves to help detect scarring of liver tissue.

**What can be done?**

No specific therapies exist for NAFLD. Instead, the focus is on treating the risk factors. To keep fatty liver disease under control, it’s usually recommended that you:

- **Lose excess weight** — Weight loss can improve and possibly even reverse fatty liver disease to some degree. Research has shown that shedding excess pounds through diet and exercise or with the help of weight-loss (bariatric) surgery can prevent further liver damage when inflammation and scarring is already present. However, any weight loss should be gradual — no more than a few pounds a week — because losing weight too quickly can actually worsen fatty liver disease.

- **Eat a healthy diet** — Eat a diet rich in fruits, vegetables and whole grains, and limit your consumption of cholesterol and saturated fats — which can be found in foods such as meat, eggs and high-fat dairy products. Cutting out fast food may be particularly helpful, according to recent research that found the high level of cholesterol, saturated fat and fructose in this type of food is associated with progressive inflammation and scarring in people with NAFLD and NASH.

- **Increase physical activity** — Government guidelines advise that each week most healthy adults get at least 150 minutes of moderate physical activity, such as walking, or 75 minutes of vigorous physical activity, such as running on a treadmill or using a step machine. Increasing that time to 300 minutes of moderate physical activity or 150 minutes of vigorous physical activity each week can yield even greater benefits, such as weight loss. A recent study of adults with NAFLD suggests that engaging in

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Health tips

Who needs vitamins?

Supplement use by healthy adults can be risky (see page 4). However, vitamin supplementation directed by a doctor may be beneficial for certain people, including those who:

■ **Have a poor or limited diet** — Whether because of a lack of hunger, no desire to cook or limited income, older adults may not eat enough. Some, such as those who have allergies, Celiac disease or kidney failure, may have a limited diet.

■ **Can’t absorb nutrients properly** — This can happen if you have celiac or Crohn’s disease or have had gastric bypass surgery. Deficiencies in vitamin B-12 and iron are common.

■ **Have a large loss of nutrients** — Chronic diarrhea or dialysis for kidney failure may deplete nutrients. Menstruation or frequent blood donation deplete iron.

■ **Can’t metabolize nutrients properly** — A number of genetic conditions can affect the ability to process nutrients.

■ **Have a condition that benefits from supplementation** — Supplementation with specific amounts of beta carotene, vitamin E, vitamin C, and zinc seems to delay the progression of the dry form of age-related macular degeneration. Alcoholism can lead to a poor diet, altered absorption and metabolism of nutrients, resulting in deficiencies of thiamin, folate and many other nutrients.

Liver transplants

When a liver becomes so damaged or diseased that it can no longer function properly, a transplant may be needed.

In the U.S., more than 6,000 liver transplants are performed each year, according to the American Liver Foundation. Cirrhosis, a condition in which scar tissue gradually replaces healthy liver tissue, is the most common reason for transplants.

Common causes of cirrhosis include heavy alcohol consumption and the hepatitis C virus. Another major cause is nonalcoholic fatty liver disease (NAFLD). With NAFLD, fat builds up in the liver. The most serious form of the disease, known as nonalcoholic steatohepatitis (NASH), can result in major liver damage in a small percentage of people.

Although it’s not clear what can cause the progression of NAFLD to NASH, fatty liver disease is considered an emerging health threat. Already, NASH is the third leading reason for liver transplantation in the U.S. and research indicates that within the next 10 to 15 years it could become the most common reason for a transplant.

vigorous activity may help reduce damage from fatty liver disease. But if you don’t already exercise regularly, talk with your doctor first about the best way to start.

■ **Manage other conditions** — If you have diabetes, high blood cholesterol or other conditions that may be contributing to fatty liver disease, work with your doctor to keep them well managed.

■ **Protect your liver** — It’s important to avoid alcohol and any unnecessary use of medication, which can put stress on your liver. If you need to take medication, carefully follow instructions and written warnings. For instance, acetaminophen — a pain reliever found in many prescription and nonprescription drugs — can cause liver damage if you take more than the recommended amount. The risk of liver injury primarily occurs when people take multiple products containing acetaminophen at one time and exceed the current maximum dose of 4,000 mg within a 24-hour period.

No alternative medicines have been found to treat NAFLD. Antioxidant vitamins have been studied to see if they can reduce or neutralize damage caused by inflammation, but results have been inconclusive. Researchers also are studying medications designed to increase sensitivity to insulin. However, questions remain about their long-term safety and effectiveness.
Risks of vitamin supplements

Most don’t help, may cause harm

Advice on vitamin and mineral supplementation is constantly changing. Over the past few years, well-conducted research has found that some supplements previously thought to be beneficial for disease prevention may not be helping — and some may actually be causing harm.

Among the latest research is an analysis of the Iowa Women’s Health Study. This tracked for nearly 20 years the supplementation habits of more than 38,000 women 55 and older. Among the findings, taking a multivitamin appears to increase risk of premature death.

With this study and others, the evidence is increasingly against taking most supplements for general health or disease prevention. There are exceptions — such as calcium and vitamin D for bone health — but even the exceptions should be approached with caution.

First, do no harm

Many people take supplements as an “insurance policy” against inadequate nutrition. However, in developed countries, deficiencies in most vitamins and minerals are extremely rare. Taking supplements provides these nutrients far in excess of what’s necessary for health.

Another reason people take supplements is to help prevent serious diseases. Studies have consistently shown that diets high in antioxidant-rich foods, vegetables and other plant foods are associated with lower rates of cancer and heart disease. However, studies looking at...
supplements haven’t shown much benefit and indicate they may actually cause harm.

Plant foods contain an array of beneficial compounds. Singling out a few specific vitamins as being beneficial appears to be too simplistic. Also, some vitamins occur in many forms — and supplements may not provide the right types in the right amounts. For example, there are hundreds of types of carotenoids that the body turns into vitamin A. There are eight naturally occurring forms of vitamin E. The B vitamins B-6, B-12 and folate also have various forms.

Potentially risky vitamin and mineral supplements include:

- **Vitamin E** — A 2005 review of research found that taking daily vitamin E supplements of 400 international units (IU) or more — and possibly even as low as 150 IUs a day — may pose health risks, including increased risk of premature death. In another study, Vitamin E and selenium were investigated for their potential to reduce risk of prostate cancer. Among more than 34,000 men 50 or older, those who took 200 micrograms (mcg) of daily selenium alone or this dose of selenium plus 400 IU of vitamin E daily saw no benefit compared with men who took an inactive substance (placebo). Men who took 400 IU vitamin E alone had a 17 percent increase in prostate cancer risk.

- **Vitamin A** — A large study of postmenopausal women found that long-term intake of at least 2,000 mcg (6,660 IU) of vitamin A acetate or palmitate may increase hip fracture risk. Other research hasn’t come to this conclusion. Supplementation with beta-carotene, a compound that’s converted to vitamin A by the body, has been shown in a large review of research to increase risk of death, especially for smokers or former smokers. Vitamin A — as retinol — is potentially toxic if taken in excess of 10,000 IU daily. Since vitamin A deficiency is rare in the U.S., it’s probably not worth the potential risk.

- **Folate an folic acid** (vitamin B-9) — Most older adults consume adequate folate. Supplementation helps prevent birth defects, but evidence of other benefits has been elusive. In fact, some research suggests that folic acid supplementation may raise colorectal cancer risk. The Iowa Women’s Health Study suggests that folic acid supplementation might increase risk of premature death by 5.9 percent. But if you were prescribed folic acid, talk to your doctor before making a change.

- **Vitamin B-6** — Large daily doses of vitamin B-6 — more than 100 milligrams (mg) — can over time cause nerve damage. In the Iowa study, vitamin B-6 supplementation appeared to increase risk of premature death by 4.1 percent.

- **Vitamin B-3 (niacin)** — High doses can help lower high cholesterol levels, but this should be done only under the supervision of a doctor. Side effects, including severe liver disease, can occur.

- **Iron** — In healthy men and postmenopausal women, iron deficiency is rare. If you’re in one of these categories and iron deficient, further evaluation may be considered. The Iowa Women’s Health Study showed a 3.9 percent increased risk of premature death among those who took supplemental iron. However, this could be considered an “ill effect” — people with anemia were told to take iron. This has been a strong criticism of this trial by some.

- **Trace minerals** — Copper, chromium, magnesium, selenium and zinc are among the essential trace minerals. However, there isn’t any solid evidence that trace mineral supplementation has any benefit in the absence of deficiency — which is rare. In contrast, the Iowa Women’s Health Study indicated that the risk of premature death increased 3.6 percent in those taking magnesium, 3 percent in those taking zinc and 18 percent in those taking copper supplements.

**What’s left?**

Supplements that older adults may consider taking include:

- **Calcium** — The recommended intake is 1,200 mg daily for older adults. Food is the best source, but you may need supplemental calcium to meet this recommendation. A recent study found that calcium supplementation increased the risk of heart attack. However, past studies haven’t supported this conclusion, and the Iowa Women’s Health Study found that the risk of premature death decreased 3.8 percent in those taking calcium. Mayo Clinic experts support meeting — not exceeding — your daily calcium requirements.

- **Vitamin D** — In support of bone health and prevention of falls, 600 to 800 IU daily from diet and supplements combined is recommended for older adults. Some doctors believe that higher doses may be appropriate. Larger daily doses should be determined from vitamin D levels in the blood. Vitamin D enhances calcium absorption.

- **Vitamin B-12** — It’s estimated that up to 15 percent of older adults are deficient in vitamin B-12. Since vitamin B-12 hasn’t been shown to cause harm, it may be beneficial for older adults to take a B-12 supplement containing 2.4 mcg — the recommended daily allowance — to help prevent deficiency.

Although many of the increased risks are small, any increase is troublesome. Because a large number of people take supplements, a correspondingly large number may experience adverse effects.
Transient global amnesia

Missing memory

Taking in a movie with your sister at the local theater is one of your regular treats. But midway through a recent movie, she asked several times why she was at the theater. When you asked if she was OK, she responded, “I’m fine,” and nabbed another handful of your popcorn.

The next day, when you mentioned the movie, she had no idea what you were talking about. She had no recollection of ever seeing the movie — or of eating your popcorn. Your observations simply confused her. She had literally dropped a scene from her life.

This type of phenomenon — though very uncommon — is a puzzling form of memory loss called transient global amnesia.

Memory interrupted

Almost any disease or injury that affects the brain can interrupt the memory. Common memory thieves include stroke, brain injury, seizures and dementias — most notably Alzheimer’s disease. Loss of past memories may also be related to psychiatric illness.

When amnesia occurs, it generally fits into two large categories:

■ Anterograde amnesia — This is the most common type and is characterized by difficulty forming new memories. It’s the type of amnesia seen in Alzheimer’s disease.

■ Retrograde amnesia — This involves the loss of past memories. Those memories may be from just a few seconds ago to several months back. For instance, it may happen following anesthesia or sedation — such as with a colonoscopy. Lost memories tend to come back over time.

A memory primer

To better understand transient global amnesia, it may help to know that memory is generally broken down into three broad types:

■ Immediate memory — This is the recall of information just seconds after learning it. For instance, a seven-digit phone number is something most people can look at, remember and dial.

■ Recent memory — This involves the recall of information several minutes or more after encountering it.

■ Remote memory — This refers to the recall of long-known information — such as where you grew up — and events months or years after their occurrence.

More-specific kinds of memory processing also come into play. For example, declarative memory involves recalling memories of past information and experiences. Procedural memory helps you remember how to do something such as drive a car.

In transient global amnesia, a combination of both types of amnesia occurs. For no clear reason, a sudden loss of recent memory occurs and the ability to form new memories is briefly derailed.

Twilight zone

When transient global amnesia occurs, it tends to be experienced by adults 50 and older. Typically, it’s short-lived, beginning and ending abruptly. Although an episode may last up to 24 hours, it’s more likely to last for six to 12 hours.

Transient global amnesia is almost always a one-time occurrence. During the event, you know who you are and can recognize people you know well. You’re also able to do complex tasks, such as drive a car. However, even though your behavior is normal in most ways, you can’t establish new memories, and your recall of recent events simply vanishes — you can’t remember where you are or how you got there. As a result, you’re likely to ask the same question multiple times.

Once the episode ends, life returns to normal with the only loss being the period during which no new memories were made.

Sorting it out

The underlying cause of transient global amnesia remains unknown, and what triggers it is up for debate. Among reported events prior to transient global amnesia are sudden immersion in cold or hot water, strenuous physical activity, emotional or psychological stress, and pain. Some have found an association with migraines.

Even though transient global amnesia is temporary, it warrants seeing a doctor immediately. Anyone who experiences a sudden change from normal awareness to confusion about what’s happening requires immediate attention.

A diagnosis of transient global amnesia rests on excluding more-serious conditions, such as stroke, seizure or head injury.

Typically, a neurological exam is done during the evaluation. Blood tests and diagnostic imaging tests — such as magnetic resonance imaging (MRI), computerized tomography (CT) and an electroencephalogram (EEG) — may be done to check for any possible abnormalities in the brain.

An episode of transient global amnesia can be disturbing, but it isn’t a predictor of future memory loss, nor a risk factor for something more serious, such as a stroke.
Treating seizures

Achievable control

There are many types of seizures. Symptoms range from staring blankly for a few seconds to a full-blown loss of consciousness with stiffening and convulsions. Regardless of your symptoms, seizures can be disruptive and necessitate treatment.

Fortunately, most people gain complete control of seizures with available treatments. However, for up to a third of people, it takes time to find the right drug option — or may even require surgery — to achieve seizure control. For those who aren’t controlled with available therapies, experimental treatments may be an option.

One time occurrence?

Two to 5 percent of people experience a seizure at some point in life. A seizure doesn’t necessarily mean you have epilepsy. If you have a seizure, seek proper evaluation. Doctors typically try to find the cause if it’s not obvious from your medical history. This may include testing to look for electrolyte abnormalities, alcohol withdrawal, infection, medication side effects, stroke or a brain tumor.

Seizures with identifiable causes are provoked seizures. If the cause is reversible, the seizures may not recur. Diagnosis of an initial seizure may involve ruling out nonepilepsy problems — such as narcolepsy or fainting (syncope) — that may cause seizure-like symptoms.

In cases where the cause can’t be found, the seizure is unprovoked. While an unprovoked seizure may be the first sign of epilepsy, 50 to 70 percent won’t have another. Because of this, the decision is often made to not treat a first seizure. However, after two or more unprovoked seizures, medication is usually recommended. After a second seizure, your risk of having a third seizure rises significantly to about 70 to 80 percent.

Medication most common

Anti-epileptic drugs are the most common therapy in treatment of epilepsy and seizures. The goal is to find the optimal dosage of a single drug that will stop seizures with minimal side effects. This is achievable for the majority of people.

If the first drug doesn’t work, others can be used in its place. However, if control isn’t achieved after trying two medications, the odds of another medication working are 10 percent or less, and referral to an epilepsy center is recommended.

Other options

About a third of people with epilepsy have seizures that medications can’t control. In such cases, additional treatment options may include:

- **Surgery** — People with partial seizures originating in one region of the brain may benefit from surgery to remove the brain tissue that triggers the seizures (the seizure focus) or to isolate that spot from the rest of the brain with a series of cuts into surrounding brain tissue. Surgery isn’t without risks. Memory impairment, speech disturbance, vision and motor function can be affected by surgery, depending on the part of the brain being operated on.

- **Vagus nerve stimulation** — This involves implanting a device similar to a pacemaker under the skin in the chest region. A wire from the device electrically stimulates the vagus nerve in the neck. This nerve allows communication between the lower part of your brain to your heart, lungs and gut. This device can reduce seizure frequency, but usually doesn’t eliminate them. It’s often used in conjunction with medications.

- **New therapies** — Researchers are continually probing new avenues of therapy for those who can’t achieve seizure control. For example, the Food and Drug Administration (FDA) recently approved ezogabine (Potiga), which is a drug that has a mechanism of action that’s different from other seizure medications. Rates of seizure reductions in the 20 to 30 percent range are modest, but may be better for some than can be achieved with other options.

Another emerging therapy is called responsive neurostimulation (RNS). This implanted device detects when a partial seizure is occurring and sends small electrical impulses that may stop the seizure. Early research has demonstrated that one year after implantation, the device can reduce seizure frequency by about 43 percent. The device is awaiting approval by the FDA.

Another emerging tool is a device that can detect impending seizures in advance of their actual occurrence. It doesn’t stop a seizure from occurring, but it alerts you so that you can prepare.
Second opinion

Q: I’ve taken aspirin for years to prevent a heart attack, and now I’ve developed an ulcer. My doctor told me to keep taking aspirin along with Prilosec. Why keep taking aspirin if it caused my ulcer?

A: Odd as it may seem to continue taking aspirin, there’s evidence that doing so while taking a prescribed proton pump inhibitor such as omeprazole (Prilosec) allows the ulcer to heal.

A recent randomized study done in Taiwan found that the peptic ulcer-healing rate was virtually the same for study participants who took a proton pump inhibitor alone as it was for those who took both a proton pump inhibitor and aspirin. An overview of 61 randomized controlled studies in the September 2011 issue of Clinical Gastroenterology and Hepatology looked at risk of gastrointestinal (GI) bleeding related to taking low-dose aspirin. The only studies in the meta-analysis that showed a reduced risk of GI bleeding were those in which participants on low-dose aspirin also took a proton pump inhibitor.

Proton pump inhibitors block acid production and promote healing. These drugs reduce stomach acid by blocking the acid pumps in the cells that normally produce acid. In addition to omeprazole, other prescription proton pump inhibitors include lansoprazole (Prevacid), rabeprazole (Aciphex), esomeprazole (Nexium) and pantoprazole (Protonix).

Q: My femur bone snapped as I was getting out of my car a couple of years ago. My doctor said that the drug I was taking to prevent fractures might have contributed to it. Why doesn’t Mayo Clinic Health Letter report this risk?

A: Mayo Clinic osteoporosis specialists say that the benefit of drugs known as bisphosphonates far outweigh the risk for most people with weakened bones or osteoporosis.

Bisphosphonates used to treat osteoporosis include alendronate (Fosamax), ibandronate (Boniva), risedronate (Actonel), and zoledronic acid (Reclast). It’s estimated that bisphosphonates prevent 30 to 50 percent of hip or vertebra fractures that would have occurred if people with weak bones weren’t taking them.

The type of fracture you may have experienced could have been an atypical femur fracture resulting from nontraumatic forces. These types of fractures are rare, accounting for no more than 1 percent of nonhip femur fractures — which make up about 5 to 10 percent of all femur fractures. In contrast, the classical femur fractures involving the hip that bisphosphonates help prevent account for 90 to 95 percent of all femur fractures.

Some studies have found an association between long-term bisphosphonate use — usually three or more years — and an increased risk of atypical femur fractures. However, a cause-and-effect relationship has yet to be proved. That’s in part because other studies have found no association between long-term bisphosphonate use and atypical femur fractures. In addition, some nontraumatic atypical femur fractures occur in people who don’t take bisphosphonates.

The Food and Drug Administration is monitoring cases of atypical femur fractures to better determine what role, if any, bisphosphonates play in causing them. Mayo Clinic experts hope this monitoring and other research provides more information about the risks of bisphosphonates so that more accurate recommendations can be made.

In the meantime, people at high risk of fractures are more likely to benefit from bisphosphonates than be harmed by them. Those who have taken bisphosphonates for three or more years should discuss with their doctors if they still need to take these medications.

Have a question or comment?

We appreciate every letter sent to Second Opinion but cannot publish an answer to each question or respond to requests for consultation on individual medical conditions. Editorial comments can be directed to:

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