

Fatty Liver Disease: More Prevalent in Children

A type of liver disease once thought to afflict primarily adult alcoholics appears to be rampant in children.

Some 1 in 10 children in the U.S., or more than 7 million, are thought to have the disease, according to recent studies.

The condition, in which the normally rust-colored organ becomes bloated and discolored by yellowish fat cells, has become so common in non-drinkers that it has been dubbed nonalcoholic fatty liver disease.

The disease's prevalence is alarming doctors who worry about its progression to nonalcoholic steatohepatitis, or NASH, when the fatty liver becomes inflamed and cells are damaged. That leads to the end stage of cirrhosis, when the liver forms scar tissue and ultimately stops working.

The condition's rise is tied to the obesity epidemic—about 40% of obese children have it—but isn't caused solely by being overweight. The disease appears to be growing among normal-weight children too, experts say.

And even though obesity rates are starting to level off, the prevalence of fatty liver disease continues to rise, they say.

It also has no symptoms, which means a person could have it for decades without knowing.

"The disease is very silent," said Naim Alkhouri, director of the Pediatric Preventive Cardiology and Metabolic Clinic at the Cleveland Clinic.

Because fatty liver disease has been recognized only fairly recently in children, it's unclear how the disease progresses into adulthood. Roughly 10% of people with fatty liver disease will develop NASH; another 15% to 20% of those will get cirrhosis. While the early stages of fatty liver disease and NASH are re-



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The Cleveland Clinic's Pediatric Preventive Cardiology and Metabolic Clinic treats and studies nonalcoholic steatohepatitis (NASH).

versible, cirrhosis is not.

"This is just really worrisome to have this number of children who have a disease this severe," said Miriam Vos, a pediatrics professor at Emory University School of Medicine who studies and treats kids with fatty liver disease.

In a study published this year, Dr. Vos and her colleagues looked at data from a national health study for elevated liver enzymes, a sign of fatty liver disease. The percentage of children in the sample suspected of having the disease grew to 10.7% between 2007 and 2010, from about 4% between 1988 and 1994.

In the last decade, more scientists have started studying fatty liver disease and NASH, trying to figure out who gets them and why. Last week, the U.S. Food and Drug Administration held a two-day meeting to discuss with industry and other stakeholders the best way to study new treatments and speed up clinical trials.

NASH, the inflamed fatty liver condition, is currently the third-most-common reason for liver transplants, behind alcoholism and hepatitis C. Experts expect it will eclipse the other two by 2030. The liver helps digest food, absorb nutrients and expel toxins from the body.

It's likely there are multiple factors that worsen fatty liver disease. Early research shows that the disease is partly genetic but likely needs to be triggered by environmental conditions, like obesity or insulin resistance. Much of the current research has focused on genes and specific nutrients in the diet that might cause the disease. One culprit is fructose, a type of sugar found in corn

syrup and fruit juice, which are widely consumed in western diets, according to Dr. Vos's research.

Some imaging studies of children born from obese women show that even the infants have more fat on their liver.

Also, certain ethnic groups, including Mexican-Americans, appear to be particularly susceptible, whereas African-Americans appear more protected against fatty liver disease, even though rates of obesity are high in the U.S. population. Scientists have discovered several genes linked to the disease. At least one, PNPLA3, appears more often in the Mexican-American population, according to Dr. Vos.

Usually fatty liver disease is detected when other health problems arise. Obesity, insulin resistance or diabetes may prompt a doctor to order blood work to determine how the liver is functioning.

Sherry Waskowski's son Gregory was 12 when he was diagnosed with fatty liver disease two years ago. He had gone to see a doctor for his long-standing acid reflux, but because he was overweight, the physician checked his cholesterol levels, blood sugar, and—unbeknown to Ms. Waskowski—his liver enzymes, his mother says. His liver enzymes came back elevated and the ultrasound that followed glowed bright, indicating an accumulation of fat.

"It was very frightening and I felt so totally responsible," Ms. Waskowski says.

The medical team educated the Waskowskis, who live in Cleveland, about the condition and what Gregory needed to do to reduce his weight, which is the primary recommendation for treatment. He now exercises five hours a week, mostly by walking on the treadmill, and eats more fruits and vegetables. The Cleveland Clinic's Dr. Alkhouri, one of his doctors, wrote a note to his school advising against excess snacking there for Gregory.

Gregory's weight is now in the normal range and his last ultrasound, in March,

showed his liver had much less fat, according to Ms. Waskowski.

There's a debate in the field about whether kids should be routinely screened for the condition and, if so, the best way to do it, Dr. Alkhoury says.

While elevated liver enzymes can be a sign of the disease, hepatitis C and other metabolic liver diseases must be ruled out first. Ultrasound helps detect the presence of fat on the liver, but is expensive. The best way of diagnosing a fatty liver is to take a sample of the liver with a biopsy, but this procedure can be painful and has side effects.

Researchers are trying to identify biomarkers detectable through breath or blood samples instead. At a major conference in the field called Digestive Disease Week, Dr. Alkhoury and his colleagues presented the results of a pilot study. It showed that different concentrations of chemicals were found in the breath of obese kids with fatty liver disease compared with those without. If the test is validated upon further study, it may be useful clinically in several years, he says.

Treatments for fatty liver disease are limited. They include weight loss through diet and exercise. Another way to battle the condition is vitamin E, an antioxidant found in supplements and foods including eggs and some leafy vegetables like spinach, that helps to reduce inflammation in adults and children with NASH, according to Joel Lavine, chief of Gastroenterology, Hepatology and Nutrition at Columbia University.

Several trials are under way for treatments for pediatric NASH. The National Institute of Diabetes and Digestive and Kidney Diseases is sponsoring one study and co-sponsoring another.

Bariatric surgery is also being studied as a possible treatment, though it's controversial because no randomized studies exist looking at NASH. Preliminary data from the Cincinnati Children's Hospital Medical Center—not yet published—suggest the procedure is very effective in adolescents with NASH, ac-

ording to Stavra Xanthakos, medical director of the Surgical Weight Loss Program for Teens there, who collected data.

"If you could mimic the effect of surgery without going through the surgery, that's where a lot of interest is," said Dr. Xanthakos.

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