



The Childhood Liver Disease Research and Education Network strives to provide information and support to individuals and families affected by liver disease through its many research programs.

ALPHA-1-ANTITRYPSIN (a-1AT) DEFICIENCY

What is Alpha-1 Antitrypsin Deficiency (Alpha-1)?

Alpha-1 Antitrypsin deficiency (Alpha-1) is an inherited disease that can cause liver problems in infants, children or adults and may cause lung problems in adults, particularly if they smoke cigarettes.

In people with Alpha-1, large amounts of the abnormal alpha-1 antitrypsin (A1AT) protein are made in the liver and nearly 85% of this protein gets stuck in the liver. If the liver is not able to break down the abnormal protein, the liver gets damaged and scarred over time. Currently, there is no way to prevent the A1AT protein from getting stuck in the liver of a person with Alpha-1. Since not all people with Alpha-1 get liver disease, there must be some other things that contribute to the liver disease, but these are not currently known. The lack of A1AT in the blood allows the lungs to get damaged by cigarette smoke and air pollution, which usually shows up in adults with Alpha-1.

What are symptoms of liver disease in Alpha-1?

Symptoms of Alpha-1 in infants can include jaundice (eyes and skin turning yellow), swelling of the liver, or poor growth. Most jaundiced infants do not have Alpha-1 or other liver problems, but have another harmless cause of jaundice. Blood tests can tell if the jaundice is due to a liver problem or the common harmless type. Diarrhea and poor weight gain may also happen in infants with Alpha-1 liver disease. Sometimes an infant or child is found to have a large liver or spleen when they are examined by their doctor or it may be found by a parent when the child is bathed. This can be caused by scarring in the liver caused by Alpha-1 and a number of other liver problems. Scarring in the liver can also lead to swelling of the abdomen by fluid (ascites), intestinal bleeding, or feeling weak and tired. These are the types of symptoms that may occur later in childhood or in adults with Alpha-1 liver disease. Most children and adults with Alpha-1 have no symptoms of liver disease at all.

How do you get Alpha-1?

Alpha-1 is a genetic condition that is passed on from parents to their children through genes. Genes are codes that are found on chromosomes, the genetic material in each cell in our bodies. Each person receives two genes for each trait in their body: one gene from their mother and one from their father. The usual (normal) alpha-1 gene is called M. People with Alpha-1 have received two alpha-1 genes that are different from the usual gene. One changed gene came from their mother and one from their father. There



are many types of changed alpha-1 genes, but the most common are called S or Z. People with Alpha-1 who could get liver disease have either two Z genes (called ZZ) or one S and one Z gene (called SZ). People with Alpha-1 who are ZZ or SZ will pass on one of these changed genes to each of their children. The alpha-1 genes tell the liver how to make the protein, alpha-1 antitrypsin (A1AT), which the liver sends into the blood so it can protect the lungs and other parts of the body.

If someone has two changed alpha-1 genes, then the liver makes a form of the protein, A1AT that becomes trapped in the liver rather than being released into the blood. The build-up of the A1AT protein in the liver can cause the liver to build up scar tissue (see below). Also, when the A1AT protein builds up in the liver, the blood doesn't get as much of the protein as it needs to help other parts of the body. This makes the lungs more sensitive to damage from cigarette smoke and other air pollutants that are breathed in.

An Alpha-1 Carrier is a person who has one normal M alpha-1 gene and one changed alpha-1 gene (usually Z or S). Most Alpha-1 Carriers are called either MS or MZ. Being an Alpha-1 Carrier is very common. Over 20 million people in the U.S. are carriers. Alpha-1 Carriers have less A1AT protein in their blood than other people, but they hardly ever have liver or lung problems. The parents of children with Alpha-1 are usually both carriers and are completely healthy.

What happens to the liver in Alpha-1?

The liver is one of the largest organs in your body. It is found in the upper right part of your abdomen. It is very important to your health because it cleans your blood and helps fight infections. The liver stores vitamins, sugars, fats and other nutrients from the foods you eat. The liver makes many substances for your body. It also breaks down alcohol, drugs and other toxic substances that can hurt your body. The liver also removes a yellow substance from the body, called bilirubin, that builds up in the blood in many liver diseases. The term "liver disease" means a number of conditions that stop the liver from working as well as it should.

Of all babies who are born with two changed alpha-1 genes (ZZ or SZ), about 1 in 20 of them will get liver disease that may be serious in the first year of life. These infants usually have jaundice (yellow color of the skin and the eyes), swelling of the liver and do not gain weight well. They may develop serious scarring of the liver. Of all infants born with ZZ or SZ, about 1 in 4 will have blood tests showing that the liver is being injured, however, the infants will feel and look fine. In most children with abnormal blood tests, the liver disease improves by itself by the time these children reach their teens, and they remain healthy. Adults with Alpha-1 can also get liver disease, usually involving scarring of the liver (cirrhosis). This is especially true for those over 50 years of age. People with Alpha-1 have up to a 30-40% chance of developing a liver problem during their lifetime. These problems include cirrhosis (scarring of the liver) and liver cancer.



If the liver does get damaged, there are treatments to prevent or slow down problems that can be caused by liver damage. Healthy living is also important. This includes avoiding alcoholic drinks, maintaining a healthy weight, getting vaccinated against infections that can damage the liver, and eating a healthy diet. If the liver damage becomes severe or life-threatening, then liver transplantation is an option.

Alpha-1 Carriers almost never develop liver problems related to Alpha-1. When they do, this is probably caused by something else that damaged the liver, like viruses, drinking too much alcohol or being overweight.

How is Alpha-1 liver disease found and diagnosed?

Alpha-1 liver disease is found by a physical exam by a doctor and by blood tests. The physical exam may show a large, firm feeling liver or spleen. The blood tests include measuring how much of the A1AT protein is in the blood and how well the liver works. In addition, ultrasound of the liver may be ordered. Ultrasound is a painless procedure using sound waves (sonor) through the skin to make a picture of the liver. The diagnosis of Alpha-1 is made by a blood test called the A1AT "phenotype" test. This test tells the type (M, Z, or S) of A1AT protein in a person's body. Doctors can also test a person's genes for A1AT from a blood sample or a mouth swab (rubbing a Q-tip on the inside of a person's mouth). A liver biopsy is usually not needed to diagnose Alpha-1. A liver biopsy is a procedure performed by a doctor, after a patient has received medicines to numb the skin and take away pain, in which a needle is pushed into the liver through the skin and a small piece of liver is removed in the needle. But liver biopsies are sometimes used to see how bad the liver disease is and to look for other reasons for liver damage.

How is liver disease treated in people with Alpha-1?

When doctors treat someone with Alpha-1 liver disease, they focus on keeping patients as healthy as they can be and preventing health problems. Treatments are available for intestinal bleeding, ascites (fluid in the abdomen), nutrition and other problems from scarring of the liver.

There is no cure for Alpha-1, but there are ways to prevent or reduce health problems related to Alpha-1. People with Alpha-1 should do the following important things:

- get hepatitis A and B vaccinations
- get regular physical exams by a doctor
- get regular medical tests as suggested by their doctors, such as blood tests and liver ultrasound exams or other X-ray tests (for example, liver CT (CAT) scans)
- stay away from tobacco smoke and heavy air pollution
- don't drink alcohol



- eat a balanced diet and maintain a healthy weight
- speak to your doctor before using any herbal, vitamin or other therapies

Severe liver damage and scarring is called "cirrhosis." In some people with cirrhosis caused by Alpha-1, the liver does not work well enough to keep them healthy and a liver transplant may be necessary. A liver transplant is surgery to remove a sick liver and replace it with a healthy one from another person.

Some adults with lung damage are treated with "intravenous A1AT replacement." This means they are given A1AT protein through a needle into a vein. This treatment is not helpful in reducing or preventing damage to the liver.

What is the outlook for someone with Alpha-1?

There is wide variation in how sick people get from Alpha-1. Some patients have serious problems if the liver is affected, while others have little or no liver disease. Some infants may have rather quick scarring of the liver that leads to the need for a liver transplantation in the first few years of life. However, this is rare and most children affected with Alpha-1 liver disease do well and reach adulthood without major liver problems. Lung problems from Alpha-1 do not occur in childhood, but it is very important for children with Alpha-1 to avoid all exposure to cigarette smoke or heavy air pollution to protect their lungs. It is best to talk with your doctor to figure out how your Alpha-1 might turn out and what can be done to protect the lungs and liver.

How can I learn more about liver disease in people with Alpha-1?

- Ask your healthcare provider
- Access information available on-line.
- Contact local, national or federal organizations and agencies dedicated to liver disease and/or Alpha-1.