Liver Disease among Adult Alphas

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Alpha-1 Antitrypsin and the Liver

- ✓ The liver makes alpha-1 antitrypsin (AAT) and releases it into the blood.
- ✓ In Alphas, AAT protein can be misfolded and get trapped in the liver.
- ✓ The buildup of trapped AAT protein leads to liver damage.
- ✓ The "Z" gene is the most common deficiency gene that leads to trapped AAT protein in the liver.
- ✓ Liver disease can be caused by many factors in addition to trapped AAT protein in the liver. These other factors include obesity, diabetes, viral infections, and alcohol use.
- ✓ Most Alphas won't develop clinical liver disease. However, liver disease is more common among Alphas than among individuals who do not have AAT deficiency.
- ✓ Liver disease is often asymptomatic, especially in the early stages.

Liver Diseases

- ✓ **Fibrosis** is scarring of the liver. The most commonly-used scoring system to describe how much scarring is in the liver is called the METAVIR stage. There are five METAVIR stages that range from:
  - ❑ Stage F0 (which indicates no fibrosis/scarring) to
  - ❑ Stage F4 (fibrosis/scarring that spans between the lobules of the liver)
- ✓ **Cirrhosis** is the term used to describe METAVIR Stage 4 fibrosis. Cirrhosis can be:
  - ❑ Asymptomatic, referred to as "compensated cirrhosis," or
  - ❑ Symptomatic, referred to as "decompensated cirrhosis," which is when portal hypertension has developed and has led to symptoms from ascites, varices, and/or encephalopathy
- ✓ **Portal hypertension** occurs when scar tissue in the liver disrupts blood flow coming into the liver, causing high blood pressure in the portal vein. The portal vein is a large vein that carries blood from your intestines and stomach to your liver. Portal hypertension can lead to:
  - ❑ **Ascites** (fluid buildup in the abdomen). Symptoms of ascites are a swollen and bloated belly.
  - ❑ **Esophageal varices** (enlarged blood vessels in the esophagus). Vomiting blood and having black stools are both signs of esophageal varices that have started to bleed.
  - ❑ **Hepatic encephalopathy** (toxins travel to the brain because the liver did not adequately clear toxins from the blood). Symptoms can range from sleepiness to severe confusion or coma.
- ✓ **Liver cancer**, while rare, occurs more frequently among Alphas than in the general population. Any disease that causes liver scarring increases the risk of developing liver cancer.
- ✓ **MASLD** and **MASH** are additional liver conditions that are highly relevant to Alphas. When fat builds up in the liver, it is called metabolic dysfunction-associated steatotic liver disease (MASLD). The advanced stage of MASLD is metabolic dysfunction-associated steatohepatitis (MASH). Alphas who have MASH and a buildup of trapped AAT protein in the liver have an additive risk for liver scarring from these conditions.

Treatment Options for Liver Disease among Alphas

- ✓ Alphas with liver disease should have a hepatologist (liver specialist) as part of their healthcare team.
- ✓ Many different medications are available to treat various aspects of liver disease.
- ✓ Currently, there are no treatments specifically for liver disease due to a buildup of trapped AAT protein. However, clinical trials are underway for such treatments. For information on currently-enrolling Alpha-1 clinical trials, visit clinicaltrials.gov.
- ✓ Liver disease can become so severe that a liver transplant is needed. The additional resources below provide information about liver transplants.

Additional Resources

- ✓ AlphaNet's Big Fat Reference Guide (BFRG) has a large section devoted to liver health. Anyone can access AlphaNet's BFRG. AlphaNet Subscribers can access the BFRG through their Subscriber Portal.
- ✓ AlphaNet has created several 1-page documents that focus on liver health, which are available here.