Alpha-1 Antitrypsin Deficiency

What is alpha-1 antitrypsin?

The enzyme trypsin is a substance in the body that is able to degrade protein. This enzyme normally performs valuable and healthy functions such as the breakdown of protein in foods. The activities of trypsin must be strictly controlled however, or it can potentially also attack normal tissues in the body causing damage. In order to control the work of trypsin and protect the body’s tissues against damage, the liver produces another substance called alpha-1 antitrypsin.

What is alpha-1 antitrypsin deficiency?

Alpha-1 antitrypsin deficiency is an inherited condition occurring in approximately one in 3,000 to 5,000 live births. In this condition, the alpha-1 antitrypsin which is produced by the body is abnormal with no protective activity and is not released in sufficient amount from the liver. As a consequence, the trypsin in the body not only breaks down proteins in foods, but also attacks various body tissues. This can lead to liver disease in young children (and occasionally in middle age) and/or lung disease in young adults.

What causes alpha-1 antitrypsin deficiency?

Alpha-1 antitrypsin deficiency is hereditary. In order to have the disease, a child must inherit two defective genes, one from each parent.

People who have only one gene for alpha-1 antitrypsin deficiency do not have the disease, but they are “carriers” of the deficiency. Their alpha-1 antitrypsin levels are lower than normal, but this does not cause any obvious health problems. In families where both parents are carriers of the gene for the disease, there is a one in four risk that a child will have alpha-1 antitrypsin deficiency.

What are the risks of developing liver disease with alpha-1 antitrypsin deficiency?

For unknown reasons, only 15 per cent of children with alpha-1 antitrypsin deficiency will develop liver disease. Of that group, about half will recover completely within the first year, while the remainder will ultimately progress to liver failure within several years.

What are the symptoms of liver disease due to alpha-1 antitrypsin deficiency?

The affected child usually presents with jaundice at a few weeks of age with enlargement of the liver and spleen and with abnormal liver function tests. A biopsy of the liver will show evidence of the stored abnormal protein and a variable degree of liver damage. If the function tests are only moderately abnormal and the biopsy does not show extensive damage, it is probable that recovery will occur and usually the infant is back to normal health by
six to nine months of age. If recovery fails, then progressive liver disease results in liver failure at some point during the first ten years of life. If this occurs, liver transplantation may be necessary. On very rare occasions, liver disease may not be evident until the child is several years of age or even until middle age.

How is alpha-1 antitrypsin diagnosed?

A diagnosis is established by demonstrating a very low level of alpha-1 antitrypsin in the blood and by identifying the abnormal protein by specific testing. In healthy individuals the normal protein is called “M”. The abnormal protein is called “Z”.

Additional tests including liver function tests, breathing tests, chest x-rays and arterial blood-gases tests should also be performed to evaluate liver and lung function in those affected.

How is alpha-1 antitrypsin treated?

Liver Disease

In rare instances where the disease progresses to liver failure, liver transplantation is the only effective treatment at this time.

Lung Disease

Over many years, injury to the lungs can result in emphysema. In some, smoking, asthma and lung infections further contribute to the development of lung problems. Typically this happens in early adulthood. For this reason, it is strongly recommended that individuals with alpha-1 antitrypsin deficiency refrain from smoking. Lung transplantation may be a last resort for treatment of severe lung disease.

In recent years, studies have been looking at the effectiveness of replacement therapy as a treatment for affected individuals showing symptoms of emphysema. The aim of replacement therapy is to increase the body's level of alpha-1 antitrypsin by infusing a blood derived product rich in this substance (alpha-1-proteinase inhibitor). The procedure is generally repeated once a week for 30-90 minutes with the aim of maintaining a level of alpha-1-proteinase inhibitor determined to protect the lung from the destructive action of trypsin. Information about the long-term efficacy of the replacement therapy on pulmonary function is not yet available, but early results look promising.

Reviewed in 2015.