Alpha-1 Antitrypsin Deficiency and Lung Disease

What is alpha-1 antitrypsin?
Alpha-1 antitrypsin is a substance present normally in the blood of all people and is essential for health. It is a protein that is made in the liver and released into the bloodstream. From the bloodstream, alpha-1 antitrypsin moves into the lungs where its work begins.

What does alpha-1 antitrypsin do?
The main role of alpha-1 antitrypsin is to protect the lungs from damage. Over the course of a lifetime, the delicate tissues of the lungs are exposed daily to a variety of inhaled materials such as pollutants, germs, dust and cigarette smoke. One aspect of the body's response as it attempts to rid the lungs of these materials is the release of enzymes by the body's cells, aimed at digesting and clearing away the harmful material. The job of alpha-1 antitrypsin, an anti-enzyme, is to contain and neutralise these enzymes before the enzymes digest the lung tissue itself.

What is alpha-1 antitrypsin deficiency?
Alpha-1 antitrypsin deficiency is a genetic (inherited) condition that may result in chronic lung and/or liver disease. An estimated 1 in 2,500 Australians inherit a genetic disorder in which the liver makes and releases too little alpha-1 antitrypsin into the blood. As a result, the level of alpha-1 antitrypsin in the lungs is too low to protect against enzyme damage.

How are the lungs affected?
The abnormal alpha-1 antitrypsin protein is trapped in the liver, causing a deficiency of the protein that would normally circulate in the blood and protect the lungs from many types of damage. The very thin walled air sacs in the lungs (the alveoli) are the most vulnerable. Over the years, the alveoli are digested away more quickly than normal, often causing emphysema by age 40 to 50. The age that symptoms become noticeable can vary widely, and is heavily influenced by environmental factors, e.g. smoking or polluted environments, working in conjunction with biology.

How is the liver affected?
Liver disorders are caused by the accumulation of the abnormal alpha-1 antitrypsin protein within the liver cells. The effects of such accumulation can range from abnormal liver function tests without symptoms to severe, symptomatic scarring (cirrhosis of the liver) and, rarely, liver cancer. Children and adults may require a liver transplant if the liver is severely affected.
What is emphysema?
Emphysema, which comes under the umbrella term COPD (Chronic Obstructive Pulmonary Disease) is an irreversible condition that results from destruction of the air sacs in the lungs. These air sacs are designed to transfer oxygen into the blood stream from the fresh air we inhale. If the air sacs are destroyed, this transfer of oxygen is reduced and breathlessness results. Cigarette smoking is the cause of most cases of emphysema. Alpha-1 antitrypsin Deficiency is rare and is the cause of emphysema in only about 2% of cases that we know of. However, smoking severely worsens the emphysema caused by alpha-1 antitrypsin deficiency. The most common symptom in emphysema is breathlessness which gets worse as the emphysema progresses. Lung Foundation Australia has published a separate COPD information brochure and a comprehensive guide called Better Living with Chronic Obstructive Pulmonary Disease: A Patient Guide.

Can I have alpha-1 antitrypsin deficiency and not get emphysema?
Yes, different people have different amounts of alpha-1 antitrypsin in their blood. Not all people will develop emphysema. The amount of alpha-1 antitrypsin present in many cases will be enough to protect the lung against destruction. Many people with alpha-1 antitrypsin levels less than 30% of normal will develop emphysema at some point during their lives. Levels above 30% of normal seem to give adequate protection unless the person is a heavy smoker or exposed to other detrimental environmental factors.

Can I relieve the symptoms of my emphysema?
Some patients find that the use of inhaled bronchodilators helps relieve their symptoms, especially breathlessness and medication options should be discussed with the doctor. It is critical to avoid cigarette smoking. Prolonged exposure to dust and fumes should also be avoided. These pollutants can cause acceleration in the rate at which lung tissue is destroyed. One of the best treatment options for patients with chronic respiratory disease is to attend a program of exercise and education called a pulmonary rehabilitation program. Lung Foundation Australia can provide contact details for these programs.

Amounts and type of alpha-1 antitrypsin in your body
The exact type and concentration of alpha-1 antitrypsin in your blood is determined by genetic messages called phenotypes. Many different phenotypes have been described in humans, but only a few cause significant alpha-1 antitrypsin deficiency. The more common examples include:

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<thead>
<tr>
<th>Phenotype</th>
<th>Alpha-1 antitrypsin Concentration</th>
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<tbody>
<tr>
<td>MM</td>
<td>Normal</td>
</tr>
<tr>
<td>MS</td>
<td>80% of normal</td>
</tr>
<tr>
<td>MZ</td>
<td>60% of normal</td>
</tr>
<tr>
<td>SZ</td>
<td>40% of normal</td>
</tr>
<tr>
<td>ZZ</td>
<td>10% of normal</td>
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The MM, MS and MZ phenotypes, which are quite common, are adequate to protect the lung against destruction. The ZZ phenotype, which is rare, is the phenotype usually associated with emphysema.

How did I inherit this deficiency?
Each parent passes one of two possible alpha-1 antitrypsin genes to their child. If one of your parents had normal levels of alpha-1 antitrypsin (i.e. phenotype MM), and the other had very low levels (i.e. phenotype ZZ), then your phenotype would be MZ (an M from one parent, and a Z from the other). In this case, you are considered to be a carrier of a defective alpha-1 antitrypsin gene but your body would produce enough alpha-1 antitrypsin to protect your lungs. If both parents have a MM phenotype, then you would be MM also. If both parents have a ZZ phenotype, then you would be ZZ also.
**Can I be treated for alpha-1 antitrypsin deficiency?**

Currently, there is no cure for alpha-1 antitrypsin deficiency. Several clinical trials of augmentation therapy with intravenous infusions of alpha-1 antitrypsin concentrate have been undertaken, and additional clinical trials are underway. This process aims to yield higher blood concentrations of alpha-1 antitrypsin, leading to improved lung protection. Several trials have shown a potential benefit for reducing the rate of progression of emphysema detected on a CT chest scan. How this translates to benefits for symptoms and lung function is not yet known. Alpha-1 augmentation therapy was approved by the Therapeutic Goods Administration (TGA) in Australia at the end of 2016, however it is not subsidised in the Australian health service.

**Looking for support and further information:**

Alpha-1 Association of Australia  
[www.alpha1.org.au](http://www.alpha1.org.au)

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