THE SYMPTOMS POINT TO COPD, **BUT IT COULD ALSO BE ALPHA-1**

From recognising to living with alpha-1

GRIFOLS

ALPHA-1: THE "GENETIC COPD"

You may not be familiar with the term alpha-1, but you probably have heard of **chronic obstructive pulmonary disease (COPD)**.

COPD defines a **group of lung problems that obstruct the airways**, making it difficult to breathe. These include emphysema, chronic bronchitis, bronchiectasis, and chronic asthma in adults.

COPD may sometimes develop due to external causes (e.g., tobacco), but it can also be **caused by genetics**, in which case it is called **alpha-1**.

Alpha-1 antitrypsin deficiency (AATD) occurs when there is a **severe lack of a protein** called **alpha$_1$-antitrypsin (AAT)** in the blood.

Alpha-1 is the major known genetic risk factor for COPD, which means that having alpha-1 makes you more likely to develop COPD.

HOW CAN ALPHA-1 AFFECT MY LUNGS?

- In a normal situation, our body secretes a protein called **neutrophil elastase**, which is responsible for eliminating irritating substances and protecting your lungs from possible damage. But if this elastase is **not controlled, it can damage your lungs**.
- The main role of **AAT is to protect the lungs from inflammation** caused by infection and inhaled irritants by **blocking neutrophil elastase**.
- If you have alpha-1, AAT is absent or deficient and not reaching your lungs to stop neutrophil elastase. This means that healthy lung tissue slowly becomes compromised over time.

HOW CAN ALPHA-1 AFFECT MY LIVER?

- **AAT is produced in the liver**. When you have alpha-1, your liver either produces no AAT or creates it in the wrong shape.
- If it is produced in the wrong shape, the **AAT protein has trouble leaving the liver**. So, not only is there less AAT in your lungs, but it is also being trapped in your liver.
- In this case, the **accumulation of a poorly shaped protein** can lead to liver tissue damage.

WHAT SYMPTOMS CAN I EXPECT WITH ALPHA-1?

Symptoms usually develop slowly. In fact, a person can have alpha-1 and not be aware of it their entire life.

The main symptoms and conditions related to alpha-1 include:

LUNGS

- Shortness of breath
- Wheezing
- Chronic cough and sputum (phlegm) production
- Recurring chest colds
- Lower exercise tolerance
- Year-round allergies
- Chronic bronchitis
- Bronchiectasis
- Emphysema

LIVER

- Eyes and skin turning yellow (jaundice)
- Swelling of the abdomen (ascites)
- Vomiting blood or passing blood in the stool
- Unexplained liver problems or elevated liver enzymes
- Neonatal hepatitis
- Chronic liver disease
- Cirrhosis
- Liver cancer

HOW IS ALPHA-1 INHERITED?

Alpha-1 is a **genetic disease**. This means if one or both of your parents have a copy of the gene responsible for AATD, you may be at risk for developing the disease, or you may be carrying a defective copy and could potentially pass it on to your own children.

Your level of risk depends on the **combination of alleles** (i.e., copies of the gene) that you carry. There are three main alleles:

- **M allele**: the normal allele. The AAT protein is made from this allele.
- **S and Z alleles**: the main defectives alleles.

If someone has a combination of one defective variant plus an M allele, they are a **carrier**.

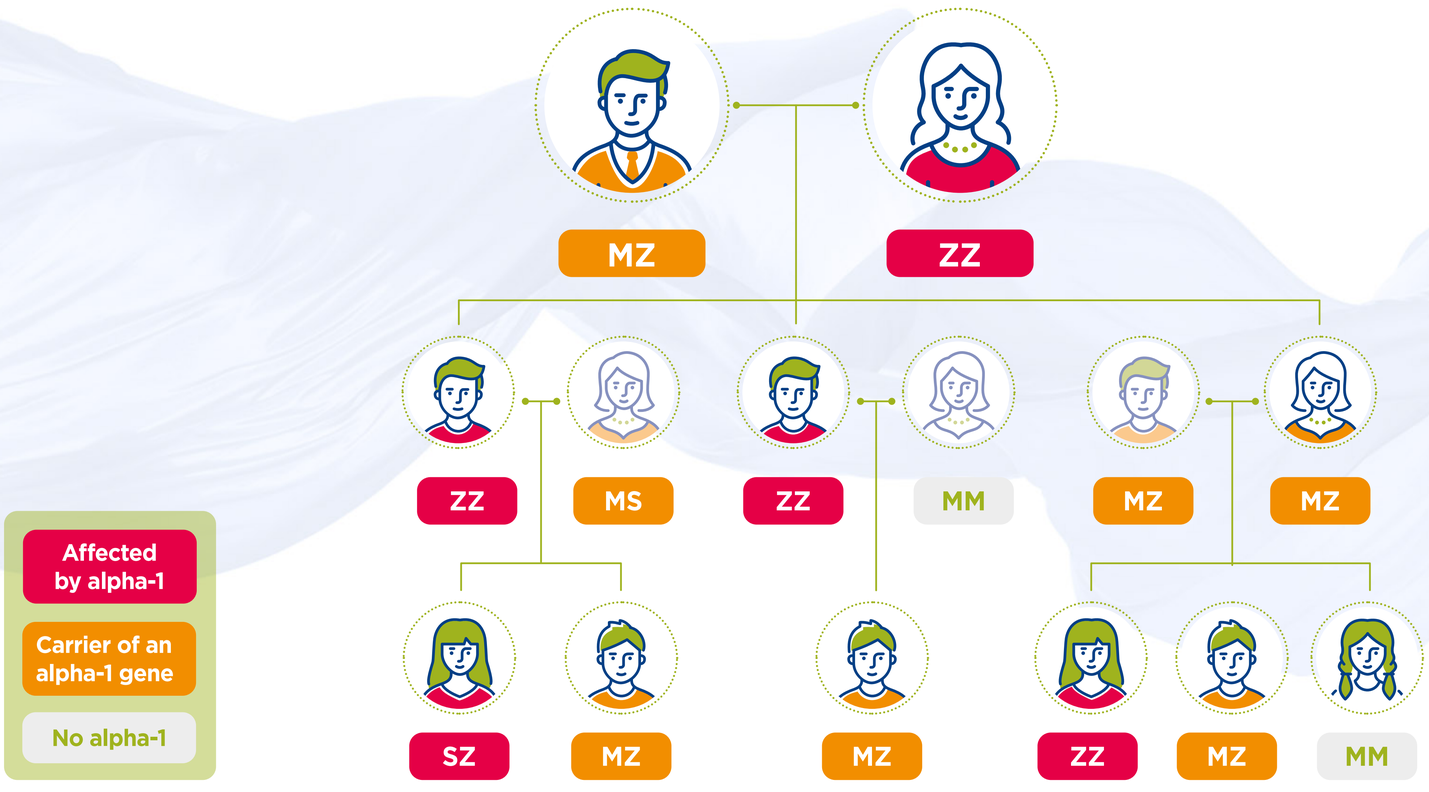
Find **here** the most frequent combinations of alleles and the risk of lung and/or liver disease.

HOW IS ALPHA-1 INHERITED?

Allele combination	Patient description	Alpha-1 levels	Risk of lung and/or liver disease
MM	Normal	Normal levels	
MS	Carrier	Normal to low levels	It is unclear whether there is a risk of getting disease symptoms, but you are carrying an abnormal AAT gene (most studies do not show an increased risk of disease).
MZ	Carrier	Low to moderately low levels	**Mild to moderate AAT Deficiency** — may get disease symptoms and you are carrying an abnormal AAT gene.
SS	Alpha-1	Low to moderately low levels	It is unclear whether there is a risk of getting disease symptoms, but you are carrying two abnormal AAT genes (most studies do not show an increased risk of disease).
SZ	Alpha-1	Low levels	**Severe deficiency** — could get the disease and you are carrying two abnormal AAT genes.
ZZ	Alpha-1	Very low levels	**Severe deficiency** — could get the disease and you are carrying two abnormal AAT genes.

combinations of alleles and the risk of lung and/or liver disease.

EXAMPLE OF HOW ALPHA-1 IS INHERITED



If you have alpha-1, then it is possible that someone else in your family has it as well.

Bear in mind that you can only see the physical symptoms of alpha-1 once damage has already occurred to your liver and/or lungs. It's important to have a diagnosis as early as possible.

WHY SHOULD I BE TESTED FOR ALPHA-1?

Getting tested for alpha-1 is a straightforward process and is **recommended for everyone with COPD** to help identify the source of their condition.

If you have been diagnosed with alpha-1, it means that your doctor now knows the main cause of your disease and, therefore, how to **best manage** it. And if the test is negative, your doctor will **rule out alpha-1** as a possible cause of your COPD and will be able to focus on looking at other causes.

There are **lifestyle changes** you can make that may help prevent further complications.

You might also be eligible for **treatment** to slow the progression of the disease.

Early detection helps to slow down disease progression.

YOUR RELATIVES CAN ALSO BENEFIT FROM TESTING

- If you have alpha-1 or carry a defective copy of the gene, **your immediate relatives** (your children, parents, brothers and sisters) are at greater risk of having the S or Z genes. **Other relatives who have lung or liver disease** are also considered at greater risk.
- Once you know your **allele combination**, you can help your family members know theirs too.
- Even carriers can develop disease symptoms and complications, which is why it is recommended that **family members are screened for alpha-1**.

In addition to patients with COPD (emphysema and/or chronic bronchitis), testing is also advised for anyone with the following medical conditions:

Bronchiectasis

Unexplained liver disease

Liver disease with a family history of liver disease

Panniculitis, a skin disease

WHAT CAN I EXPECT FROM TESTING?

The testing process for alpha-1 is fairly **simple**, **quick** and **highly accurate**. So, you can reassure your family members in case they have uncertainty about the process.

The diagnosis of alpha-1 is usually determined by a **blood test**; however, genetic testing can also be done through a **mouth swab test**.

Testing for alpha-1 is simple and will help you and your family know if they are at risk.

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Click for more info

Consume alcohol with caution, if at all

Click for more info

Avoid exposure to occupational and environmental pollutants

Click for more info

Create a nutrition programme

Click for more info

Develop an exercise program

Click for more info

Maintain mental health and well-being

Click for more info

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Close

Smoking significantly increases the risk and severity of emphysema and decreases your lifespan considerably.

Consume alcohol with caution, if at all

Avoid exposure to occupational and environmental pollutants

Create a nutrition programme

Develop an exercise program

Maintain mental health and well-being

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Consume alcohol with caution, if at all

Close

If you have any indication of liver damage, you should avoid alcohol completely.

Avoid exposure to occupational and environmental pollutants

Create a nutrition programme

Develop an exercise program

Maintain mental health and well-being

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Consume alcohol with caution, if at all

Avoid exposure to occupational and environmental pollutants

Close

Occupational and environmental pollutants (particle pollution) can irritate your lungs and cause or worsen lung problems. They can also be absorbed through the skin and thus damage the liver.

Create a nutrition programme

Develop an exercise program

Maintain mental health and well-being

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Consume alcohol with caution, if at all

Avoid exposure to occupational and environmental pollutants

Create a nutrition programme

Close

Salt and protein intake may become a concern because fluid retention is common. Keep this in check with the help of a nutritionist.

Develop an exercise program

Maintain mental health and well-being

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Consume alcohol with caution, if at all

Avoid exposure to occupational and environmental pollutants

Create a nutrition programme

Develop an exercise program

Close

It is important to exercise muscles in the chest and upper body that are related to breathing as well as the large muscles of the legs.

Maintain mental health and well-being

WHAT CAN I DO TO IMPROVE MY HEALTH?

If you are diagnosed with alpha-1, you will need to take extra care of your health. Here are some **tips** to help you feel better.

Quit smoking and avoid second-hand smoke

Consume alcohol with caution, if at all

Avoid exposure to occupational and environmental pollutants

Create a nutrition programme

Develop an exercise program

Maintain mental health and well-being

Close

Learning relaxation techniques can help you have a more optimistic outlook on life and may prevent depression.

WHAT TREATMENTS COULD I RECEIVE?

Although there is **no cure for alpha-1**, there are ways to **prevent or reduce lung or liver problems related to alpha-1**.

In addition to benefiting from lifestyle changes, if you have a lung and/or liver disease, you should seek medical help. There are different treatment options, depending on your specific condition.

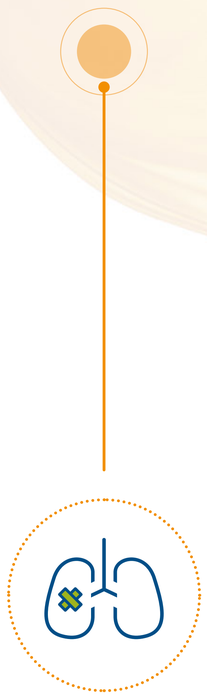
VACCINATIONS

- It is very important for you to have **annual flu shots**.
- Consider that **Prevnar vaccine** should be given once and not within one year of a **Pneumovax vaccine**.
- Discuss with your doctor if you need the **hepatitis A or B** vaccines.
- Make sure to get **fully vaccinated against COVID-19**.

WHAT TREATMENTS COULD I RECEIVE?

LIVER DISEASE

- **Large volume paracentesis:** to remove large volumes of fluid from the abdomen.
- **Banding or sclerotherapy of veins in the esophagus:** to reduce bleeding from the veins.
- **Portal vein decompression:** to reduce the pressure in blood vessels entering the liver from the digestive organs.



LUNG DISEASE

- **Antibiotics:** used at the first signs of a lung infection (coughing up yellow-green mucus or phlegm) to fight against the infection.
- **Bronchodilators:** administered via inhalers to improve lung function and allow better airflow.
- **Corticosteroids:** to reduce inflammation within and around the airways to improve lung function.
- **Supplemental oxygen:** to help patients with low blood oxygen levels.
- **Surgery:** removing part of the damaged tissue (lung volume reduction) or replacing one or both lungs (transplantation).
- **Augmentation therapy:** to restore AAT to normal levels.

WHAT IS AUGMENTATION THERAPY?

The goal of augmentation therapy is to **increase the level of alpha-1 protein in the lungs**. Augmentation therapy is usually given to individuals with **documented emphysema and severe alpha-1** (defined as individuals with two abnormal alpha-1 genes).

It is important to know that this treatment option is not a cure: it will not reverse lung damage that has already occurred nor treat or prevent liver problems related to alpha-1.

DOSING AND ADMINISTRATION

- The therapy is administered by a **weekly 60 mg/kg** intravenous infusion and is considered ongoing and lifelong.
- The infusions are normally **administered by healthcare professionals**.
- You can choose to **self-infuse at home** after receiving appropriate instructions from a healthcare professional and approval from your doctor.

BEFORE TREATMENT

- Before starting the infusions, you may be tested to see if you have an **IgA deficiency**. Don’t worry, testing is normal: it is to avoid possible serious allergic reactions to plasma-derived products.
- It’s also recommended to receive **immunisations against both hepatitis A and B** in order to reduce the risk of liver injury.

POSSIBLE SIDE EFFECTS

Patients receiving any of the available augmentation therapies have reported a variety of side effects, although **the vast majority don’t experience any significant problems**.

The most common side effect is a sense of **feeling drained** or having **flu-like symptoms** that typically last for up to 24 hours after an infusion.

Other patients have mild **allergic-like reactions**: rash, itching, chest tightness, dyspnea and/or wheezing.

WHERE TO FIND ADDITIONAL SUPPORT

- Whether you are thinking about getting tested or have already been diagnosed, there is more helpful information available.
- The area where you live may have support groups and/or patient organisations that can offer you guidance and support. Patient organisations are the best place to share experiences and to learn more about living with AATD.

You can find out if there is a support organisation in your country here:
www.alpha-1global.org

Additional information and resources about alpha-1 can be found here:
https://www.alpha1.org/

GRIFOLS

GNL-UBD-2100089