uncover alpha-1

COULD YOUR LUNG CONDITION BE GENETIC?

A GUIDE TO UNDERSTANDING ALPHA-1 ANTITRYPSIN DEFICIENCY (ALPHA-1)

Up to 30% of people with COPD (chronic obstructive pulmonary disease) or asthma **may have an underlying genetic cause**, such as Alpha-1, for their lung disease.

Takeda

Uncover the basics of Alpha-1

Alpha-1 antitrypsin deficiency (Alpha-1 for short) is a genetic condition

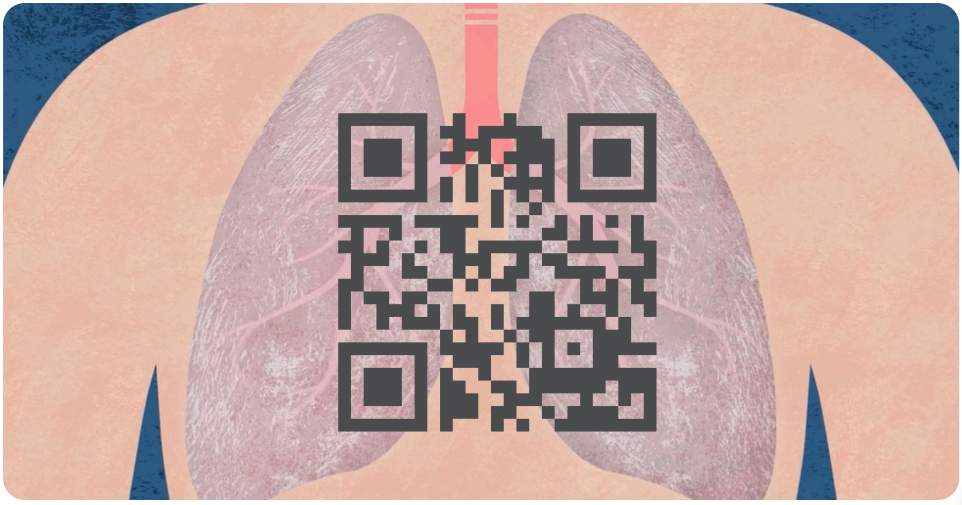
Does lung disease run in your family? If so, genetics may be the cause.

Alpha-1 is a genetic condition in which the body is unable to supply enough Alpha-1 antitrypsin proteins to the lungs. Without enough of these proteins, you may be at increased risk for COPD, emphysema, asthma, or other serious lung conditions. Even if you are an active smoker, genetics may also be an underlying cause for your lung condition.

Alpha-1 can be passed from one generation to the next through abnormal forms of the Alpha-1 gene. Genes are made of a type of information called DNA that gets passed along to you by your parents. The Alpha-1 gene determines how your body produces the **Alpha-1 antitrypsin (AAT)** protein, which is made in the liver.

When it functions correctly, the AAT protein circulates in the bloodstream and helps protect the lung tissues. People who do not have enough AAT proteins, or have misshapen AAT proteins, may be at risk for developing certain lung and/or liver conditions.

Scan the QR code below to see what Alpha-1 does in the body



Uncover the basics of Alpha-1 (cont'd)

Why there might not be enough working AAT proteins in the body

There are **3 main reasons** why there might not be enough functional AAT proteins:

1. The liver creates misshapen AAT proteins that can get trapped in the liver and can't easily move into the bloodstream toward the lungs.
2. The liver doesn't make enough (or make any) AAT proteins.
3. The liver produces AAT proteins that don't function the way they should.

When one of these things occurs, there is higher risk for COPD, asthma, emphysema, and other serious lung conditions and/or liver disease.

Alpha affects about 1 per 3000 to 5000 people, but of the estimated 100,000 affected Americans, less than 10% were diagnosed.*

**Based on the 2003 ATS-ERS (American Thoracic Society and European Respiratory Society): Standards for the Diagnosis and Management of Individuals with Alpha-1 Antitrypsin Deficiency*

Who should get tested for Alpha-1?

Do you have any of these symptoms or risk factors?

If you've had any of the experiences listed below, check the box next to it—and remember to discuss it with your doctor.

- ☐ I have COPD or emphysema with no known underlying health risk or condition
- ☐ I have an immediate family member (parent, sibling, child) who has been diagnosed with Alpha-1
- ☐ I have chronic, uncontrolled asthma, bronchitis, or year-round allergies
- ☐ I have a liver disease without any known causes
- ☐ I have raised, tender skin spots that form ulcers (a skin condition called necrotizing panniculitis)

Both the ATS-ERS (American Thoracic Society and European Respiratory Society) and GOLD (Global Initiative for Chronic Obstructive Lung Disease) recommend testing based on criteria like the above.

For this genetic condition, early testing is important

Understanding your genetics means more than just knowing your family history—which is why your doctor may suggest testing.

If your body can't produce enough AAT proteins, your lungs may be more easily damaged by irritants. This can lead to serious lung disease, which is permanent, and can keep getting worse. **That's why early diagnosis is so important.**

! **On average, it takes 7 years from symptom onset to being diagnosed with Alpha-1***

**Based on a survey of 300 individuals*

Who should get tested for Alpha-1? (cont'd)

A quick blood test is all it takes

Your doctor may order a simple, quick blood test that can be done at your doctor's office. One blood draw can be used to **learn 3 things about Alpha-1**.

1. **The Serum Level**
   The amount of AAT protein in your blood

2. **The Phenotype**
   The physical characteristics of the Alpha-1 gene, and whether the type or amount of the AAT protein is abnormal

3. **The Genotype**
   The specific type of Alpha-1 genes you inherited. Every gene, including the Alpha-1 gene, is made of 2 alleles—one from each parent. The word "allele" is used to describe different forms or versions of a gene.

With 1 blood draw, your doctor can determine whether you are at an increased risk of developing certain lung conditions related to Alpha- 1, or whether Alpha-1 could be passed to your children.

Your overall health is important

Depending on your results, your doctor may consider more testing. This could include pulmonary function testing (PFT) to determine the health of your lungs, as well as a CT scan or x-ray of your lungs.

Ask your doctor about getting tested for Alpha-1

Get to know the Alpha-1 gene

Be aware of how Alpha-1 runs in families

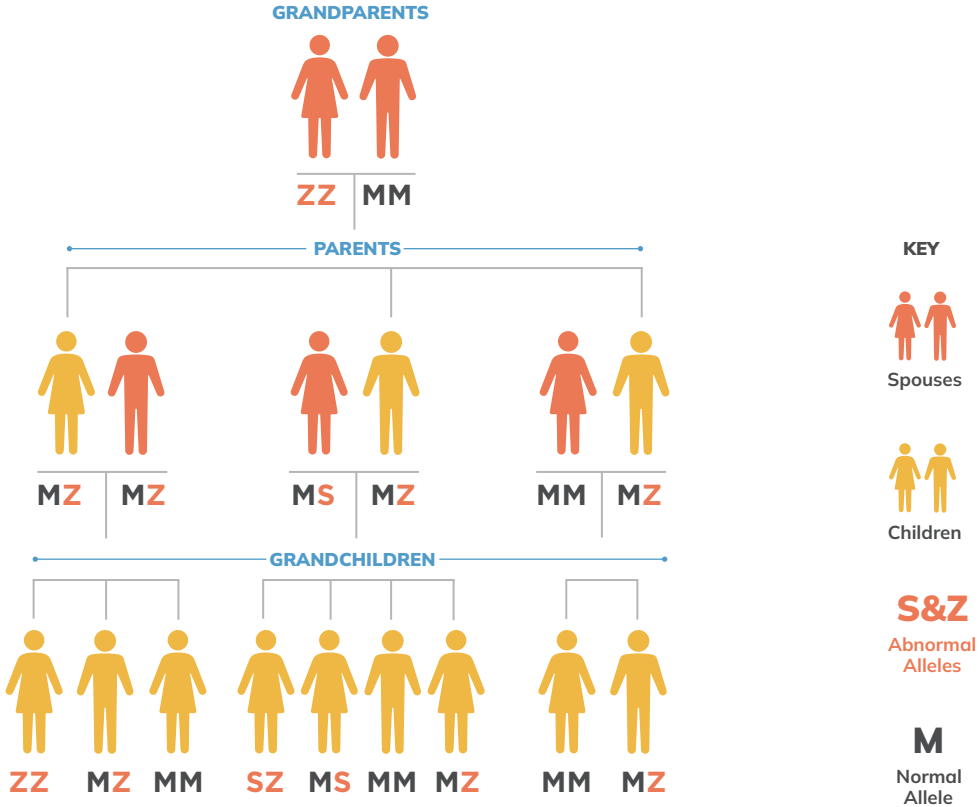
This family tree shows the three most common forms of Alpha-1 alleles:

M allele: produces normal levels of AAT protein

S allele: produces moderately low levels of AAT protein

Z allele: produces very low levels of AAT protein

Here's an example of what may happen when 2 Alpha-1 carriers pass along different combinations of their Alpha-1 alleles to their children:*



More than 100 different types of Alpha-1 alleles have been identified. Your doctor can identify which alleles you have with a blood test.

Get to know the Alpha-1 gene (cont'd)

What your genotype means for developing lung or liver conditions

When your doctor tests you for Alpha-1, they'll be able to learn your genotype. Knowing your genotype means **knowing which combination of alleles** (that make up the Alpha-1 gene) **you inherited from your parents**. Depending on your genotype, you may have a higher risk of certain conditions. Look at the list below to compare the differences.

Based on your genotype and levels of AAT proteins, talk to your doctor about how best to manage your condition.

Genotypes and their potential risks:

- **ZZ:** a higher risk of COPD and liver disease (even if you don't smoke)
- **SZ:** a relatively low risk of lung or liver disease (unless you smoke)
- **SS:** a relatively low risk of lung or liver disease
- **MZ:** a higher risk of COPD (especially if you smoke) and some risk of liver disease

"It's important to get tested because when you have that knowledge, you can move forward."

*-**Julie**, living with Alpha-1*

What are the options for managing Alpha-1?

Work closely with a doctor

Your management options may vary depending on the type and severity of lung disease and/or liver disease and associated symptoms. You can work with your doctor, including various specialists, to explore what type of management plan makes the most sense for your specific needs.

One or more of the following types of doctors might be a part of **your Alpha-1 healthcare team***:

Primary care physician
(may also be called a family physician)

Gastroenterologist/hepatologist
(specializes in liver disorders as well as the pancreas and gallbladder)

Pulmonologist
(specializes in diagnosing and treating lung diseases)

Allergist/immunologist
(specializes in allergies and/or health issues caused by immune system problems)

**These are just some examples of the type of doctors who could help you manage Alpha-1, but there may be others.*

What are the options for managing Alpha-1? (cont'd)

Options to help manage your health with Alpha-1 include:

Environmental & lifestyle changes

- Avoid exposure to dust and fumes.
- Quit smoking, vaping, and stay away from secondhand smoke.
- Get regular exercise and do breathing exercises.
  - Exercise alone won't reverse lung disease, but it can help with how you feel, breathe, and function. Even doing light exercise like going for a walk or taking a gentle yoga class can go a long way. Make sure to check with your doctor before starting any new exercise program or activity.

Medications

- **Inhaled medications** (for example, fast-acting or rescue inhalers) can help open the airways in the lungs.
- **Antibiotics** may be needed when lung infections occur.
- **Augmentation therapy** works over time to help increase the levels of AAT proteins in your body.
  - It's something your doctor may prescribe if you have severe Alpha-1 antitrypsin deficiency with emphysema.
  - This type of therapy is made from human plasma and is given through an infusion that goes into a vein (called *intravenous*).
  - You may be able to get your infusions at an infusion center, a doctor's office, or at your own home. The long-term effects of Alpha-1 replacement and maintenance therapy have not been studied.

Takeda has 2 options for augmentation therapy available. Talk to your doctor about what might be right for you.

What are the options for managing Alpha-1? (cont'd)

Oxygen therapy

- Receiving extra oxygen through a mask or tube can help if your oxygen levels get too low.

Illness prevention

- Preventative strategies are recommended to help protect you from developing illnesses that affect the lungs. These strategies involve things like maintaining healthy hygiene and staying current on vaccinations, including:
  - Annual flu shot
  - Pneumococcal (pneumonia) vaccination for older adults
  - COVID-19 vaccination
  - Washing your hands often
  - Using alcohol-based hand sanitizer to kill germs

Ask your doctor about what may be right for you.

Ready to start talking about Alpha-1?
Write down questions for your doctor here.

Let's Discuss Alpha-1

Alpha-1 is a genetic condition that can result in lung damage—which is why it's important to have discussions with your doctor about testing, management, and more.

Check your symptoms

Since the last time you met with a doctor, have you experienced any of the following symptoms (circle one)?

Shortness of breath YES NO

Excessive cough with phlegm or sputum production YES NO

Wheezing YES NO

Persistent, year-round allergies YES NO

Chest pain that increases when breathing in YES NO

Identify your risk factors

Review the list below and select any factors that may put you at risk for Alpha-1:

I've been diagnosed with one of the following:

- COPD YES NO
- Asthma YES NO
- Emphysema YES NO
- Chronic Bronchitis YES NO
- Bronchiectasis YES NO

I have an immediate family member (parent, child, or sibling) who is diagnosed with Alpha-1 YES NO

I have unexplained liver disease or a family history of liver disease YES NO

I've had ongoing exposure to lung irritants (such as smoking, vaping, pollution, dust, and fumes) YES NO

Ask your doctor questions about Alpha-1

No matter where you are in the Alpha-1 journey, it's important to have open conversations and work closely with your doctor.

How do you test for Alpha-1?

Do any of my family members need to get tested?

Should I visit a specialist (pulmonologist, allergist/immunologist, or gastroenterologist/hepatologist)?

What lifestyle changes should I make?

What medication or therapy options may be a good fit for me?

What foundations or community groups can I go to for support?

Talk to your doctor about Alpha-1 and visit **UncoverAlpha1.com** for more information.

US-NON-8517v1.0 10/22