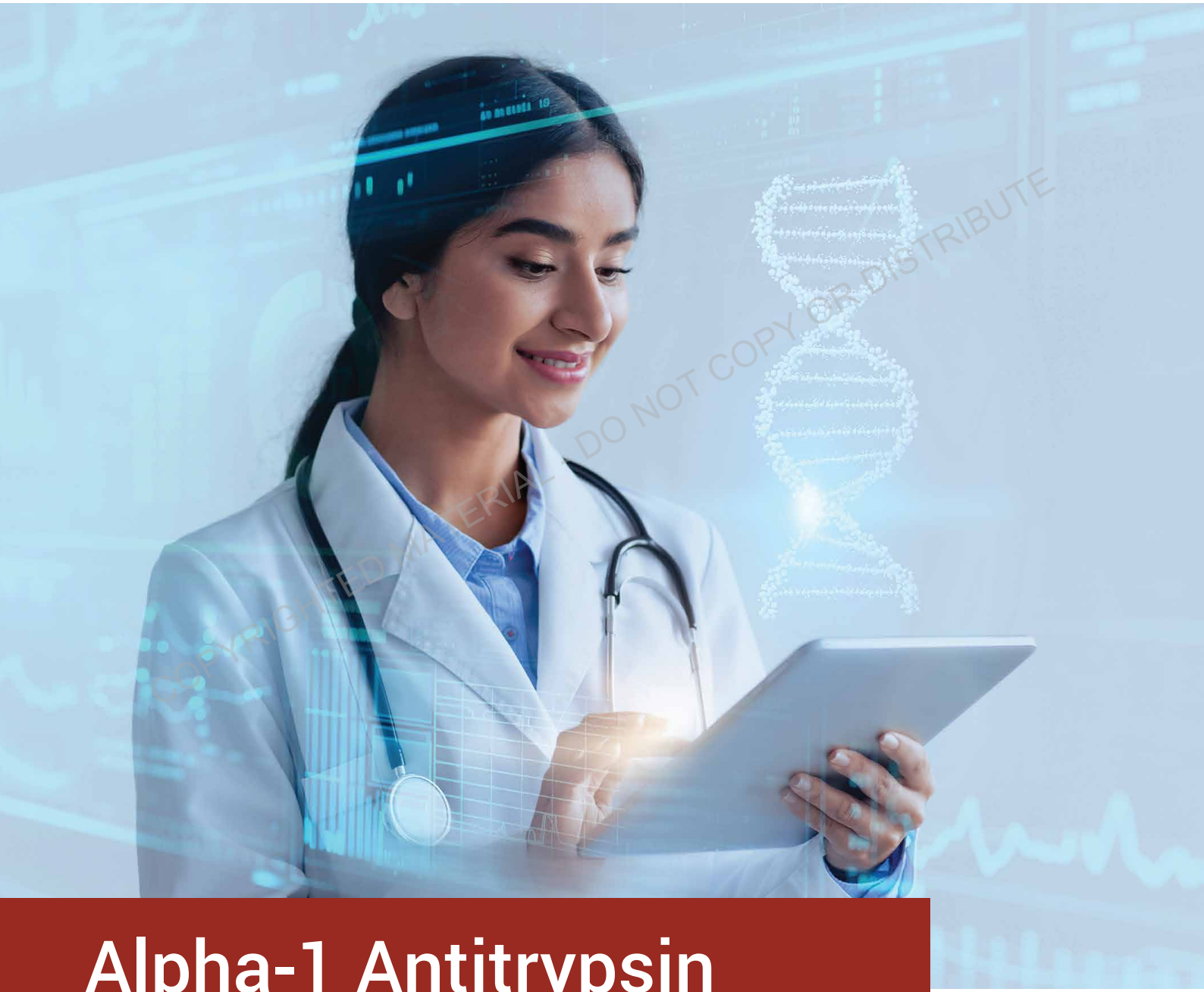
Living Well with COPD™



Alpha-1 Antitrypsin Deficiency (AATD)

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The skills you need to manage your COPD

Chronic obstructive pulmonary disease, or COPD, is a disease that can seriously affect every part of your life. As the disease progresses, it can take a toll on your daily activities. Fortunately, there is a lot that you can do to try and manage these limitations and improve your well-being. This is why we have created this series of workbooks on COPD self-management.

How can this program help me with the self-management of the disease?

This module is part of the Living Well with COPD program. It is an educational program in which you learn skills to help manage your disease and adopt healthy new lifestyle behaviours. The Living Well with COPD program has been tested in several clinical trials and the results were very encouraging. Patients who used these workbooks in collaboration with their healthcare worker, "case manager" or resource person and physician had fewer exacerbations requiring hospitalizations or emergency room visits. Their quality of life has also improved, enabling them to do more of the activities they enjoyed, and better cope with their disease.

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National and international guidelines agree that self-management education is extremely valuable for individuals with COPD. The Living Well with COPD Self-Management Program, which you can adapt to your own situation, was created by medical experts in collaboration with COPD patients.

This is your guide. Use it to write down your questions or concerns. Share it with people close to you so that they can understand what you are going through. Discuss whatever thoughts and feelings you have with your case manager or resource person and your physician.

Good luck with your program!

Dr. Jean Bourbeau
Montreal Chest Institute,
McGill University Health
Centre (MUHC)

Maria Sedeno BEng, MM
Executive Director
RESPIPLUS

Introduction to the AATD module of the Living Well with COPD series

In this learning module we will discuss Alpha-1 Antitrypsin Deficiency (AATD). There may be many reasons why you are reading this today. It may be possible that you or someone you love has been recently diagnosed with this condition. Or maybe you want to learn more about how AATD plays a role in the development of COPD.

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How did you hear about AATD?

Have you been recently diagnosed?

In this module you will learn more about:

- What AATD is and its genetic (hereditary) basis.
- The potential consequences of AATD.
- How AATD is diagnosed.
- How AATD is treated.
- What to do to live well with AATD.
- Organizations that can provide more information and support.

If you have COPD and you have not yet been tested for Alpha-1 Antitrypsin Deficiency, you can ask your family doctor or your respiratory physician about appropriate testing.

Table of contents

Section 1: Understanding AATD

- What is Alpha-1 Antitrypsin Deficiency? 2
- What is the genetic basis of AATD? 4
- What are the effects of AATD? 5
- AATD in the lungs 5
- AATD in the liver 6
- Assessment of lung and liver disease 7
- Who needs to be tested? 8
- Diagnosing AATD: What is involved? 9
- Importance of an early diagnosis of AATD 12
- Genetic testing considerations 13

Section 2: Living Well with AATD

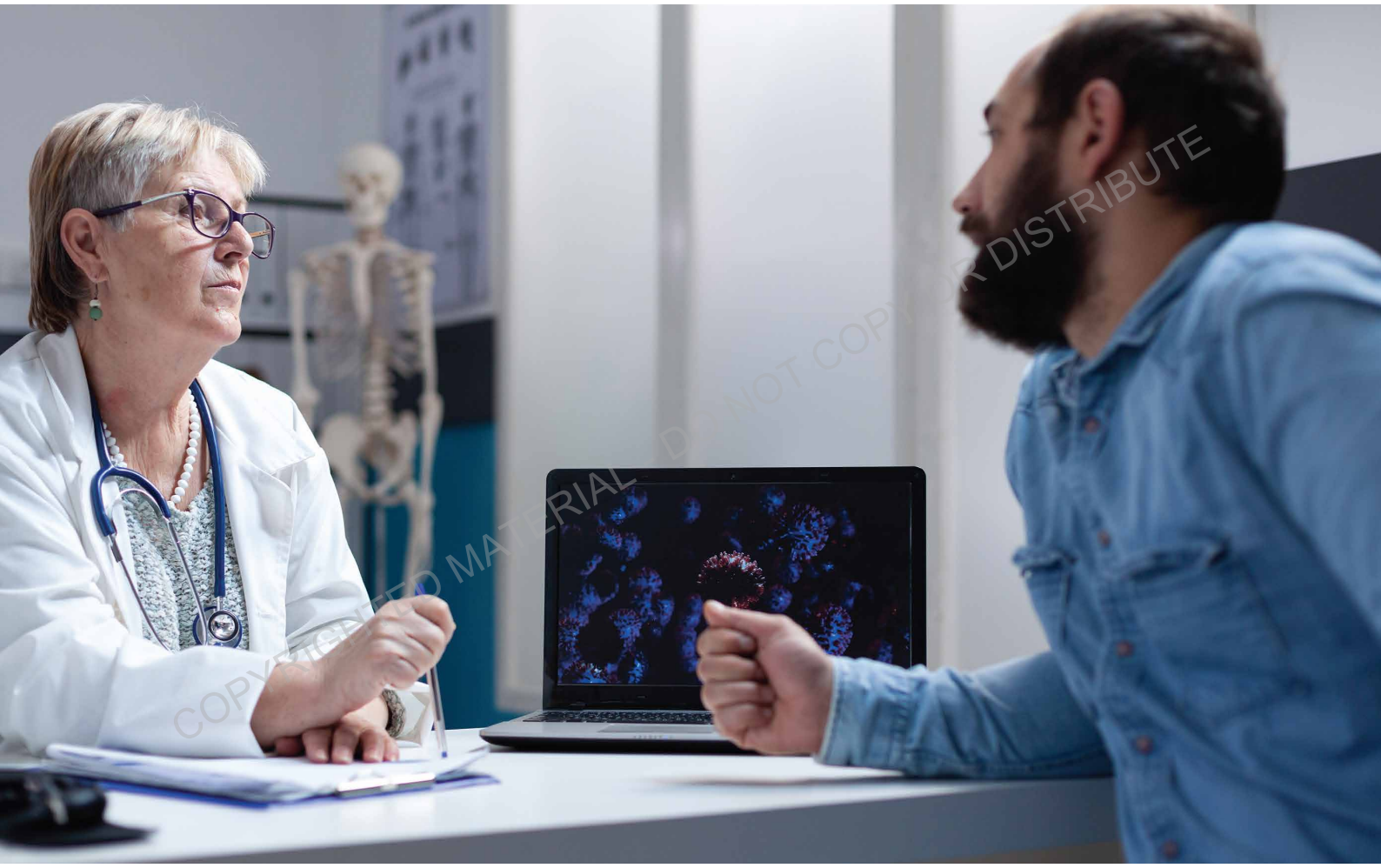
- Living Well with AATD 15
- Treating AATD: Augmentation therapy 16
- Dealing with the Impact of AATD 18
- Resources 21
- Glossary 24

Section 3: Appendices

- Appendix 1: Understanding the process for AATD diagnosis 26
- Appendix 2: Where can I be tested? 27

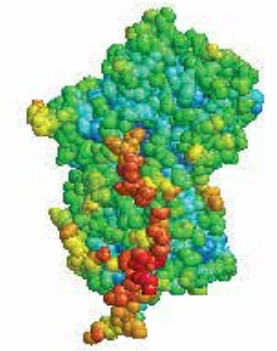
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Understanding AATD


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What is Alpha-1 Antitrypsin Deficiency?



Alpha-1 antitrypsin deficiency (AATD) is a genetic hereditary condition that can lead to lung (e.g. COPD) and liver problems. It happens when the liver does not produce enough protein called alpha-1 antitrypsin.

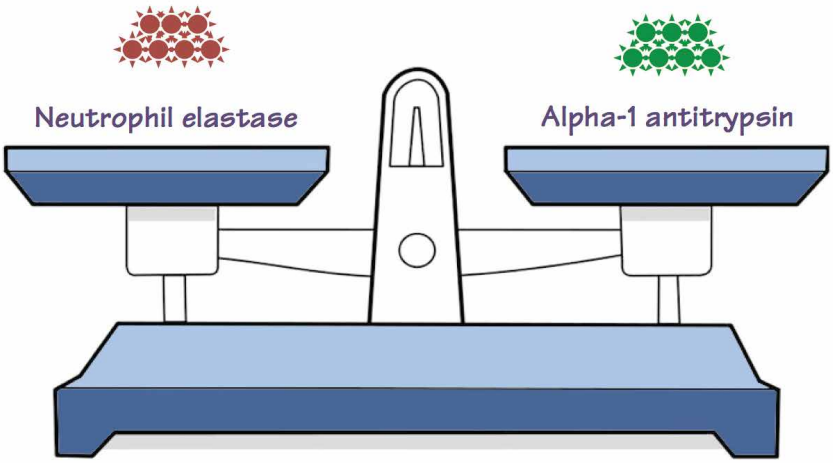
What is AAT?

AAT is a protein produced mainly in the liver and released into the bloodstream. It's main job is to protect the tissues in the body from damage caused by the enzyme neutrophil elastate.

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What is neutrophil elastase?

Neutrophil elastase is an enzyme (a type of protein) that helps kill bacteria. It can also damage the tissue (e.g. in the lungs). This enzyme is normally cancelled out or balanced by AAT.



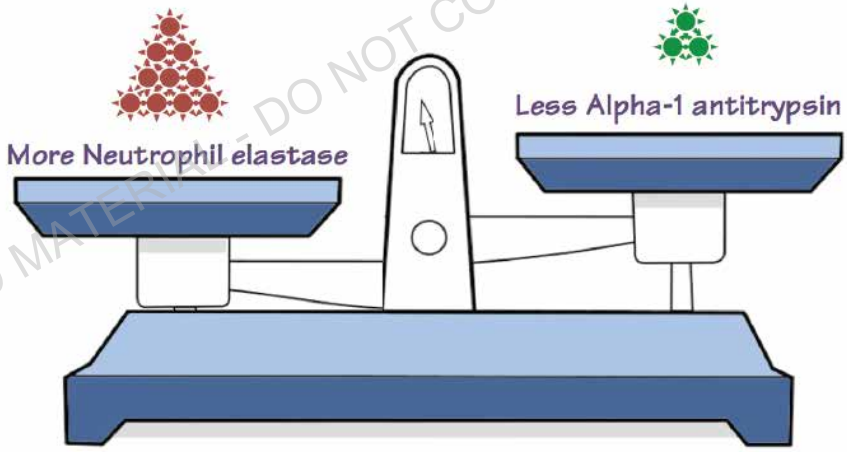


What happens if there is an imbalance between AAT and neutrophil elastase?

Neutrophil elastase increases during respiratory infections and will also increase in response to environmental exposures such as cigarette smoke or pollution.

When you do not have enough AAT to cancel out the increase in neutrophil elastase, the lungs are damaged and that can lead to emphysema.

- Bronchopulmonary infections
- Pneumonia
- Cigarette smoke or pollution
- Alpha-1-Antitrypsin Deficiency



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What is the genetic (hereditary) basis of AATD?

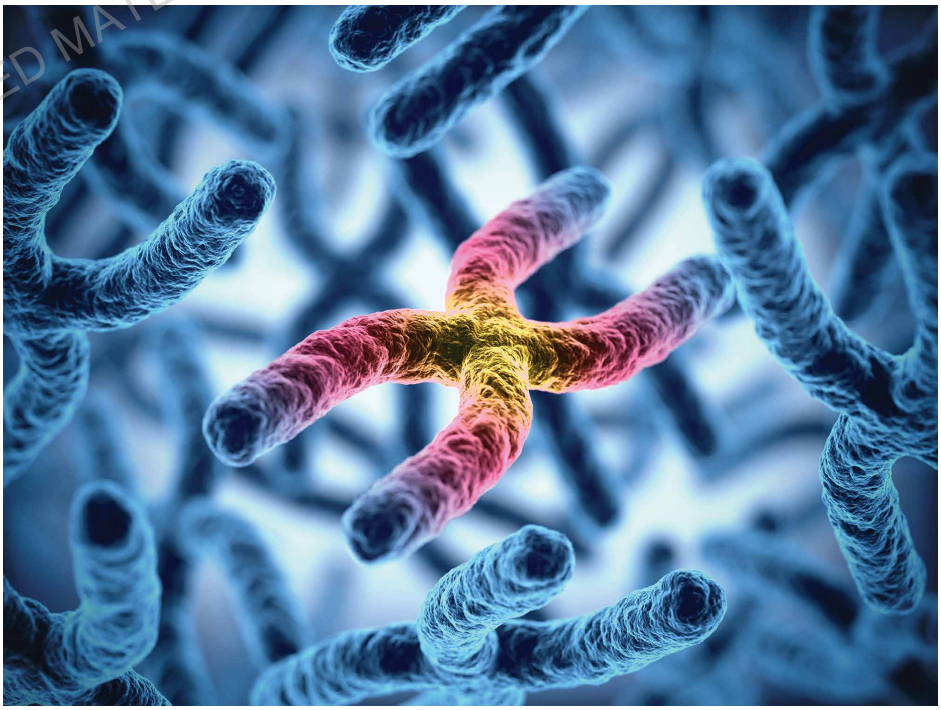
Genes are instructions that tell our bodies what to do.

AATD is caused by one or more genes you inherited from your parents not working properly.

You get a copy of the AAT gene from each parent. It is possible to get one damaged copy of the AAT gene, or two damaged copies. When you get one damaged copy of the gene, you should be able to produce enough AAT to live a healthy full life, especially if you don't smoke.

If you have two damaged copies of the AAT gene, you may not be able to produce enough AAT, which means the lungs and liver can become easily damaged.

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What are the effects of AATD in the Lungs?

Although it can develop in non-smokers, emphysema in AATD is most frequently related to smoking and other environmental exposures (e.g. pollution). Many individuals with AATD never develop the disease.

- Emphysema: This is the most common lung disease related to AATD. When the quantity of AAT that reaches the lungs is low, the lungs are more vulnerable to the harmful effect of tobacco or other environmental exposures, resulting in emphysema at a younger age and/or to a more severe degree. Emphysema is a lung disease that is part of a group of lung problems called chronic obstructive pulmonary disease (COPD). In emphysema the tiny air sacs in your lungs are damaged making it difficult to breathe.
- Bronchiectasis: Bronchiectasis is a dilatation (enlargement) of the bronchi (main airways in the lungs) leading to accumulation of secretions, cough, phlegm and more frequent respiratory infections.

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Respiratory symptoms of AATD appear during adulthood, while liver symptoms are more frequent in children.





What are the effects of AATD in the Liver?

As we have seen, AAT is produced in the liver cells. AATD causes AAT protein to accumulate in the liver, which can cause liver diseases.

Liver disease is related to an accumulation of the AAT protein and therefore, AAT augmentation therapy is not helpful and is not used.



- Neonatal jaundice: Newborns can have inflammation of the liver (hepatitis) that leads to the accumulation of a pigment (bilirubin) which causes a yellow coloration of skin and mucous membranes.
  More severe liver involvement can occur, and liver disease caused by AATD is a common cause for liver transplantation in children.
- Hepatitis and cirrhosis: As well as appearing in childhood, significant liver disease occurs mostly in adults, due to long-term accumulation of AAT in the liver. Many people affected choose to avoid alcohol consumption to minimize their risk of additional liver damage.

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Other

Other less frequent diseases that have been related to AATD are panniculitis (a skin condition) and vasculitis (inflammation of the blood vessels).



Assessment of lung and liver disease

The tests and their frequency during follow-up will be determined by your doctor based on your previous results.

After the diagnosis of AATD, your doctor may do some tests to assess your lung condition and check for possible liver disease.

- To determine if emphysema/COPD are present, it is recommended to perform full pulmonary function tests (breathing tests) and a CT scan of the chest.
- To determine if liver disease is present, a blood test will be performed. In some cases, you may also go through an imaging test of the liver (e.g. an echography, etc.).

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Who should be tested?

Testing for AATD is recommended in the following cases:

1. COPD, emphysema, chronic bronchitis or asthma that is not controlled after optimal treatment.
More specifically, those younger than 65, or everyone with minimal exposure to cigarette smoke (someone who has smoked less than a pack a day for 10 years).

2. Other situations such as:
- A family history of early emphysema with or without a smoking history,
- A family history of liver disease,
- A skin condition known as Panniculitis, and
- Newborns, children, adults with unexplained liver disease.

3. Blood relatives, especially siblings and children, of those diagnosed with AATD.

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If you have not yet been tested for Alpha-1 Antitrypsin Deficiency, you can ask your family doctor or your respiratory physician to perform this important test.





Diagnosing AATD: What is involved

Step 1 – Measuring AAT levels (screening test):

A simple blood test detects the level of AAT circulating in your blood. If your AAT levels are normal, it is less likely that your lung condition is associated with AATD and it is usually not necessary to perform other tests (unless there is a high suspicion from your healthcare provider).

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Diagnosing AATD: Understanding the process

If your AAT levels are low, it does not automatically mean that you have AATD.

Step 2 - Genotyping (identifying your genotype):

The diagnostic must be confirmed with a genetic study which looks at the differences in your genes. This is performed using a technique called polymerase chain reaction (PCR).

Genotyping only identifies the most common gene differences.

Step 3 - DNA Sequencing:

When your genotype cannot be determined by PCR, your doctor might ask for a DNA analysis containing all the available genetic information on the gene (DNA sequencing). This technique is the gold standard, and it provides the definitive genetic diagnosis. It is only performed in a few centers in Canada.

Once you know your AAT levels and genotype, it is not necessary to repeat those tests.

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For more information on the testing process and where you could be tested, please consult Appendices 3 and 4.



What do the results mean?

The risk of developing lung or liver disease varies for each genotype:

- Lung disease is associated with low AAT levels.



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- Liver disease is associated with the accumulation of the AAT protein in the liver.





Why is an early AATD diagnosis important?

An early diagnosis of AATD is very important. It allows you to:

- Make lifestyle changes: Knowing that you have AATD can be the motivation to quit smoking (or in some cases, never start), to change your working enviroment, to exercise more, to improve your diet, etc.
- Perform screening tests for your family members: if you have AATD, your family members (siblings, children) can be tested. Even if they are not sick they should start to integrate changes in their lifestyle to prevent getting sick (such as quitting smoking).
- Receive specific treatment: in addition to regular medication for COPD, some people might benefit from AAT augmentation therapy which is the specific treatment for emphysema related to AATD (see treatment section, page 16).

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Genetic testing considerations

In Canada, when buying insurance, companies can ask you for permission to contact your doctor for copies of your medical records.

You might consider genetic counseling before having your genotype or DNA sequencing.

A positive test for Alpha-1 antitrypsin deficiency could represent an abnormal medical condition which may affect your insurance coverage.

People affected by AATD and family members are often reluctant to consider genetic testing for fear the finding of a genetic abnormality will jeopardize their future insurability.

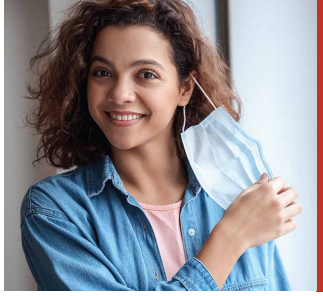
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- The concern is common although Canada has recently enacted legislation that aims to protect against insurance companies using the genetic information of their clients.
- Family members reluctant to request a screening test should know that the brothers and sisters of a severely deficient individual have a 25% risk of the same genetic problem.
- Children of a person with a severe deficiency are unlikely to have the same problem as their parent because they receive one gene from their other parent and odds are that it will be normal. Most such children are carriers. Children can be screened indirectly by testing their non-AATD parent.
  Consider confidential genetic screening.

Living Well with AATD



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Living Well with AATD

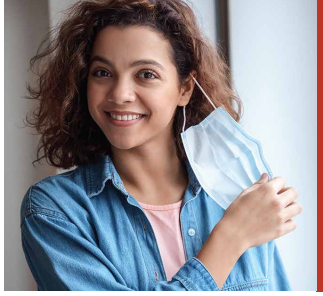
Your doctor has identified that you have AATD and that your COPD is related to this genetic condition. You may wonder what happens next. The primary goal is to slow down the progression of your COPD with prevention and treatment. Additionally, by making healthy lifestyle choices, you can limit the impact of this condition on your life.

There are four major components in the treatment of AATD:

Each of these components will be covered in detail in the following sections.

1. Preventing exposure to factors that may damage your lungs, with the goal of reducing symptoms and slowing down disease progression. This includes living in a smoke and pollutant-free environment.
2. Improving the pharmacological and non-pharmacological treatment of COPD as much as possible. An important part in managing your AATD and COPD is to take your medication as prescribed by your doctor. Adherence to your prescription and using the proper inhalation techniques can be a key for success. The nonpharmacological treatment includes implementing lifestyle changes such as being active and eating healthy.
3. Using augmentation therapy, which is the specific medication for people who have AATD. We will discuss this treatment used to slow down the progression of the disease.
4. Managing "flare-ups" or worsening of symptoms: Prevention and early intervention is key. Developing a written action plan with your physician and healthcare team is one of the best strategies to help you recognize and manage early a worsening of your symptoms.

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Treating AATD: Augmentation therapy

At the time this module was published, Health Canada has approved three augmentation therapies in Canada to treat AATD: Prolastin-C® (Grifols Canada Ltd.), Glassia® (Takeda Canada Inc.), Zemaira® (CSL Behring Inc.).

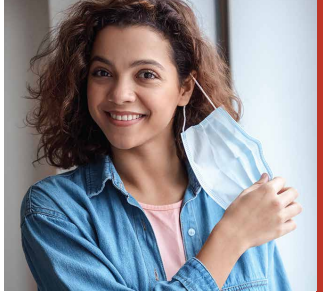
Augmentation therapy is the weekly intravenous (IV) infusion of Alpha-1 Antitrypsin (AAT) protein that has been purified from the blood of human donors with normal levels of AAT.

The only existing treatment for AATD is called Augmentation Therapy.

1. This therapy increases AAT protein levels in the blood and has been shown to slow down the progression of emphysema in people with severe AATD.
2. Augmentation therapy is not a cure, and will not reverse lung damage that has already occurred. The goal of therapy is to slow down the progression of the disease.
3. Augmentation therapy does not treat liver problems related to AATD. Your doctor will tell you if you are a good candidate for augmentation therapy, based on your emphysema, genotype and AAT level.
4. This medication is affected by tobacco usage, and cannot be given given to those who are currently smoking. If you are an active smoker, now is the perfect time to begin your journey towards a healthy tobacco-free life. Please refer to the module "Living Well Smoke Free" for more information on this topic.

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The goal of augmentation therapy is to slow down the progression of emphysema.



Access to Treatment

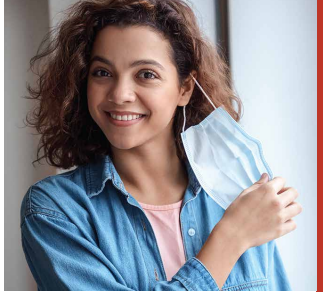
In 2024, Canada became the first country to provide an Alpha-1 Proteinase Inhibitor (A1-PI) through a national blood operator for patients with severe Alpha-1 Antitrypsin Deficiency (AATD).

An A1-PI class has now been added to the Canadian Blood Services' Plasma Protein and Related Products (PPRP) Formulary for adult patients with severe Alpha-1 Antitrypsin Deficiency and clinical evidence of emphysema, provided they meet the following criteria:

- A respirologist has confirmed the diagnosis of severe AATD and clinical evidence of emphysema and has determined that the patient would benefit from A1-PI therapy.
- A1-PI deficiency is defined as serum A1-PI levels of <11 µM/L or <57 mg/dL before initiating treatment.
- The patient has clinical evidence of emphysema (FEV1 <80%).
- The patient has been a nonsmoker for at least six months.
- The patient has not undergone a lung transplant.

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As of this publication, adult patients with severe Alpha-1 Antitrypsin Deficiency (AATD) residing in Québec continue to have access to an Alpha-1 Proteinase Inhibitor (A1-PI) through private third-party insurance and/or the Régie de l'assurance maladie du Québec (RAMQ).



Dealing with the Impact of AATD

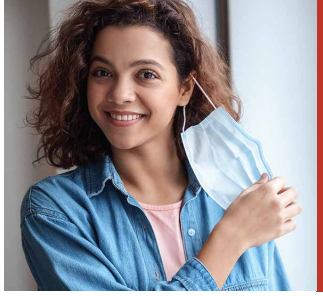
What worries you most about being diagnosed with AATD?

Do you know someone who has AATD? If so, have you spoken to that person about it?

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AATD can have an impact on different aspects of your life.

- Overtime, you may feel the impact of AATD on your shortness of breath. Some tasks and activities that used to be simple, are now more difficult to accomplish, for example, climbing stairs. As discussed in previous sections, it is very important to try and keep active to avoid further deterioration in your muscles. You can also learn some techniques to help you control shortness of breath in the module “Managing your breathing and saving your energy” from this series.
- Knowing that this disease is genetic can cause a feeling of guilt towards your children and the anxiety of having passed it on to them.
- The course of the disease and the response to the treatment can lead to anxiety and a feeling of uncertainty. Not knowing what the future holds for us can prevent us from enjoying life and setting goals.



Dealing with the Impact of AATD

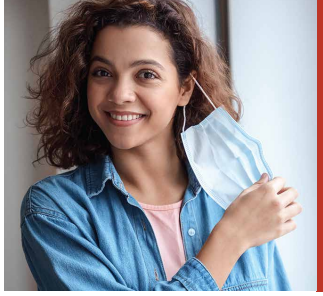
Talk to your doctor during your medical visits. Share your concerns. Prepare your questions in advance. You may also contact the organizations listed on the Resources section.

You can also try talking to a mental health professional like a psychologist about your fears or concerns. Support groups do exist for people affected with AATD.

The Lung Health Foundation has a National Support group: https://lunghealth.ca/support-resources/virtual-and-call-in support-group/

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It is important to talk to your family, for example, your brothers and sisters, as well as your children, so that they can prevent the onset of respiratory problems and get tested.



Let us here the story of Isabelle

I always assumed that feeling winded was just part of getting older. For years, I brushed off my constant breathlessness as a sign of normal aging and even mild COPD. Every time I struggled to catch my breath during a simple walk or while doing chores, I would tell myself it was nothing serious. But deep down, I felt there was something more going on.

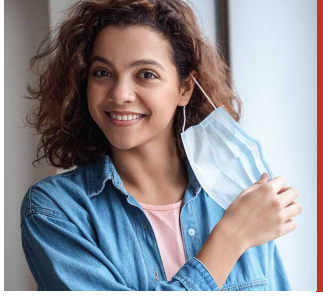
My wake-up call came one afternoon when I was climbing a set of stairs at home and suddenly felt as though I couldn't get enough air. My heart pounded, and I had to pause, feeling completely overwhelmed. That moment pushed me to seek more answers. After several visits and tests that led nowhere, a caring specialist finally suggested testing for Alpha-1 Antitrypsin Deficiency (AATD). I remember the mix of shock and relief when the diagnosis came through. Shock, because I had never heard of AATD before, and relief, because finally, there was an explanation for the constant struggle I'd been enduring all these years.

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The diagnosis wasn't just about me—it turned out that AATD runs in families. My doctor advised that I encourage my family members to get tested too. It was a difficult conversation to have, worrying that my loved ones might face the same challenges, specially my two daughters. But it was essential. Knowing our family history has allowed us all to be more proactive about our health (and it helped one of my girls to finally quit smoking).

Another turning point was joining a pulmonary rehabilitation program. At first, I was a bit skeptical about whether exercise and group sessions could really make a difference. But the rehab program taught me practical ways to manage my breathing and build strength. What really helped was hearing other patients share their own journeys. Their stories made me feel understood and less alone in this battle. Short phrases like "You're not alone" echoed through the sessions, lifting my spirits when I needed it most.

Today, with proper treatment, lifestyle adjustments, and the continued support of my rehab group, I feel like I'm finally reclaiming my life. I'm more active, more hopeful, and better equipped to handle each day. This journey has been long and full of ups and downs, but every step has brought me closer to a healthier, more fulfilled life. And for that, I am incredibly grateful.



Resources

AlphaNet Canada

AlphaNet Canada

Focused on providing health management services to individuals who have been diagnosed with, and are living with AATD, AlphaNet Canada follows up with people who are currently infusing augmentation therapy, or have prescriptions for augmentation therapy but have not been able to obtain it due to health insurance issues. AlphaNet Canada also follows those who are diagnosed with severe AATD and who do not have a prescription for augmentation therapy. AlphaNet Canada's services are free to all with AATD in Canada.

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- Contacting patients at least once each month to ensure that lines of communication always remain open and support is provided as needed.
- Providing education about AATD and how to live healthier lives through proven disease management techniques.
- Sharing information about current clinical trials (research protocols).
- Connecting patients to AATD resources.
- All of AlphaNet Canada's Disease management coordinators are trained individuals who have AATD themselves.

http://www.alphanetcanada.ca/

Contact an AlphaNet Coordinator at:

http://www.alphanetcanada.ca/coordinators/

Check your confidence level

On a scale of 1 to 10, circle the number that best represents the confidence that you have in your ability to apply the strategies and techniques learned in this module.

1. To discuss with your physician about getting the necessary tests to better understand your disease?

1 2 3 4 5 6 7 8 9 10

not at all confident very confident

2. To have an open discussion with your physician and healthcare team about appropriate treatment decisions?

1 2 3 4 5 6 7 8 9 10

not at all confident very confident

3. To be involved in your treatment decisions (for example having an action plan)?

1 2 3 4 5 6 7 8 9 10

not at all confident very confident

4. To make the necessary changes in your lifestyle to better manage your disease?

1 2 3 4 5 6 7 8 9 10

not at all confident very confident

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In summary...

We hope that this module has been helpful and it has provided you a comprehensive overview of AATD as well as the knowledge and tools to live well with this condition.

It is important to remember that you can manage your disease successfully with the help of your physician and healthcare team: routine visits to your lung specialist, taking your medication as directed, being aware of the signs and symptoms of any exacerbations or "flare ups" and treating them early.

Remember the importance of healthy lifestyle choices, such as living in a smoking-free environment, healthy eating and regular exercise.

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Glossary

- AAT: Alpha-1 Antitrypsin is a protein produced in the human body. The main function of AAT is to protect the lungs and other organs from inflammation caused by infections, smoking, pollution, etc.

- AATD: Alpha-1 Antitrypsin Deficiency is an hereditary disease consisting in low levels of AAT or a protein dysfunction.

- DNA Sequencing: In AATD, sequencing allows to look at the entire genetic code for the gene producing AAT. This technique is very specific and can find any known abnormal genes. The limitation is that in certain circumstances there is no way to know whether any new gene abnormalities are significant (there can be changes in the gene that cause no problems). Sequencing is only performed in a few centers.

- Gene: a gene is a "unit" or a piece of genetic information. It contains the "instructions" or "recipe" to make a protein, for example, AAT.

- Genotype: combination of genes; refers to your genetic identity. This term can be used to refer to the whole genetic information of an individual, but it also can refer to a particular gene or group of genes (such as in the AATD genotype).

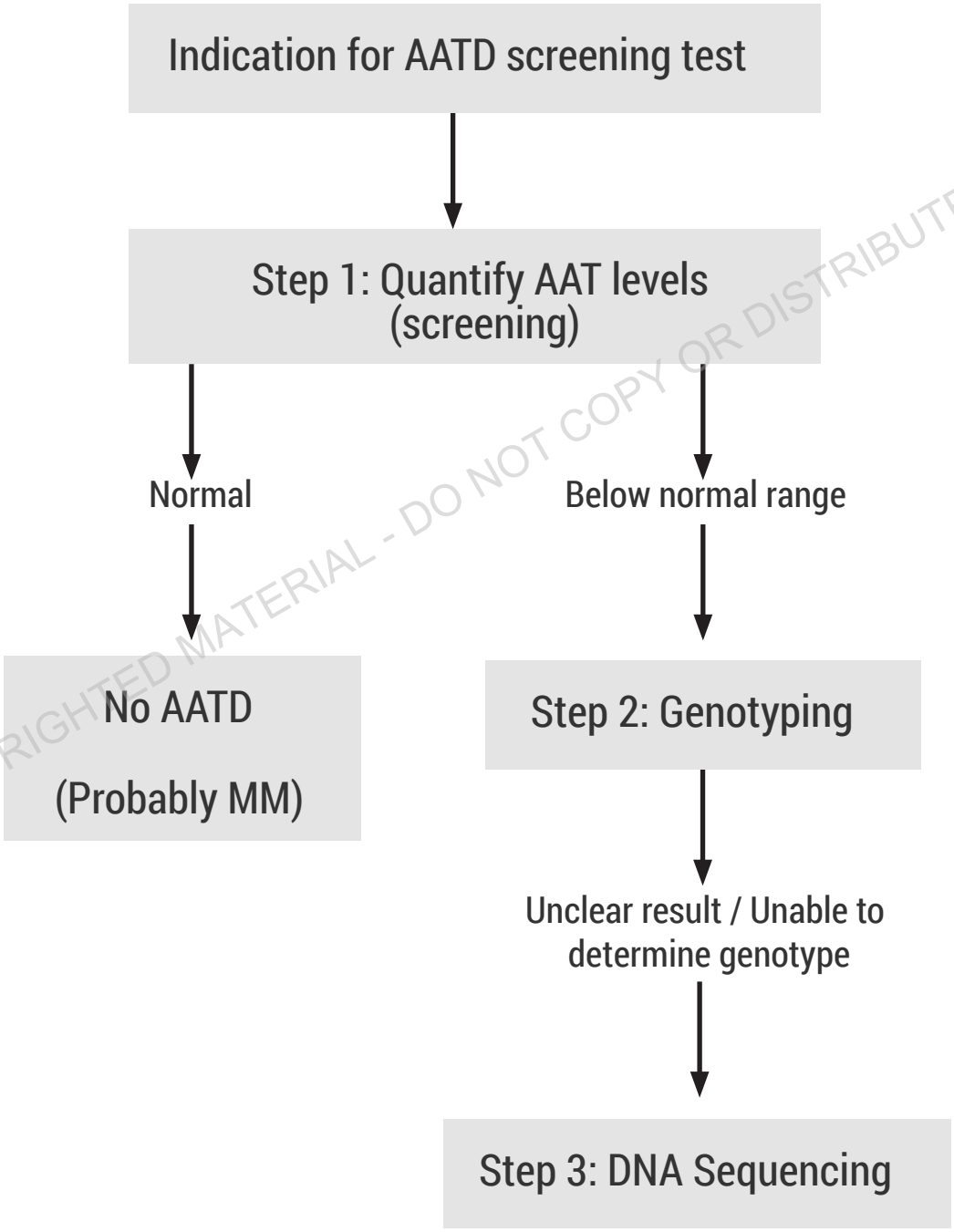
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Appendices



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Appendix 1: Understanding the process for AATD diagnosis



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Appendix 2: Where can I be tested?

Step 1 – Quantifying AAT levels

The quantification of AAT levels by taking a blood sample is accessible and can be ordered from any clinic (general practitioner, internal medicine, pneumology...). Confirmatory testing is widely available to all Canadian physicians. It is important to note that these test results will appear in your medical records. Anonymous testing is available by contacting AlphaNet Canada.

Step 2 – Genotyping

If your AAT levels are low and you need further testing:

- Your doctor can refer you to a Respirologist.
- Your doctor can order an Alpha-1 test kit.
  - You will receive the test kit by mail.
  - You will provide three small blood drops on a sample paper (dried blood sample) that you will mail to a testing facility called GeneAidyx (postage paid, pre-addressed envelope for the testing facility is provided).
  - Within four to six weeks the registry will receive the results and contact you immediately, at no cost.

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Step 2 & 3 – Genotyping and DNA Sequencing

This is used to observe the AAT genes and test them for common abnormalities. There are a number of laboratories in Canada that do genotyping and sequencing.

Acknowledgements

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Participating Institutions

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J. Bourbeau, respirologist
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"A trend to increase the autonomy of the patient in the management of its own medical situation… I saw an invitation to get involved… We are moving towards an extremely important shift in the relationship between the patient and the doctor."

H. Tremblay, expert patient

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