alpha-1 ORGANISATION AUSTRALIA INC

Alpha Times

Newsletter of Alpha-1 Organisation Australia inc *Issue 18 Spring 2024*

From the President's Pen

I hope you are well and enjoying the change of season. In Australia, depending on where you live, different seasons can cause a range of symptoms and issues for people affected by Alpha-1 Antitrypsin Deficiency and in this edition, we explore the impact of Spring.

As you may know we aim to bring key information to light including information on clinical trials that can improve quality of life, delay symptom progression, improve longevity and provide a cure such as DNA and RNA emerging therapies.

Previous newsletters have explored clinical trials in detail and if you missed these you will find them on our website a1oa – www.a1oa.org.au.

Thank you to members who attended our recent annual general meeting (AGM) and helped to make it a success. Charity members should have received an email copy of the 2024 Annual Report with the AGM papers. If you don't have a copy of the report, you will find it on our website, along with a new publication "Liver Questions You Could Ask Your Doctor" (under the Resources tab). As Alpha-1 patients can experience different symptoms and health issues, I encourage you to explore the questions in this new liver resource and choose any relevant questions. We hope to release a similar publication called 'Lung Questions You Could Ask Your Doctor'. If you would like to **suggest additional fact sheets on other topics,** please email suggestions to me at pres.a1oa@gmail.com

I love Spring and am looking forward to some outdoor activities. I hope you enjoy the next few months and that Spring doesn't impact too much! Stay safe everyone.

Wishing you all the best,
Gaynor Heading
President A1OA

Mental Health First Aid

Alpha-1 Organisation Australia has an accredited Mental Health First Aider who is ready to help if you are not coping after a diagnosis of A1AD for yourself or a family member. A new diagnosis can cause mental distress, anxiety, or depression. Please reach out to mentalhealth.a1oa@gmail.com

Spring is sprung
The grass is ris
Pollen's in the air.

I start to cough
I start to sneeze
I'm feeling quite unwell.

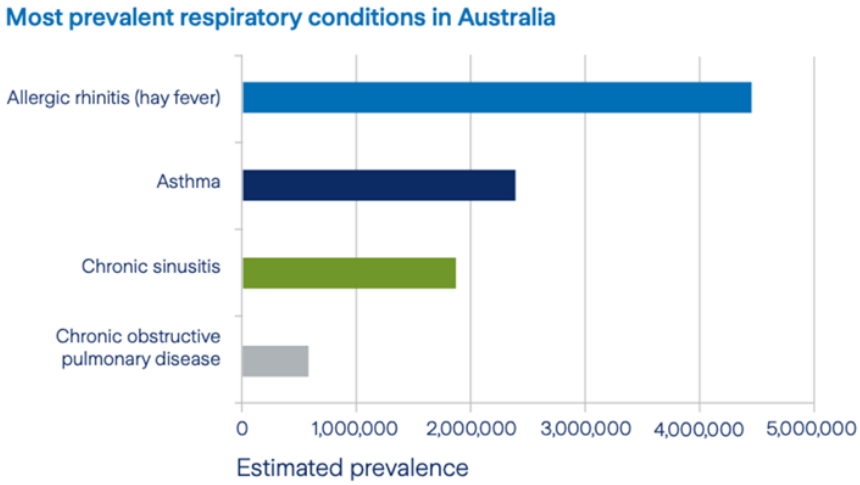
The watering eyes
The runny nose
It really is unfair.

The way I feel
The struggle's real
When pollen's in the air.

Leonie Robison

Spring is here and we are enjoying the warmer weather. For many, though, this is allergy season. Many of us with Alpha-1 Antitrypsin Deficiency (AATD) suffer from allergic conditions, such as hay fever, or allergic rhinitis as it is more properly called, and asthma.

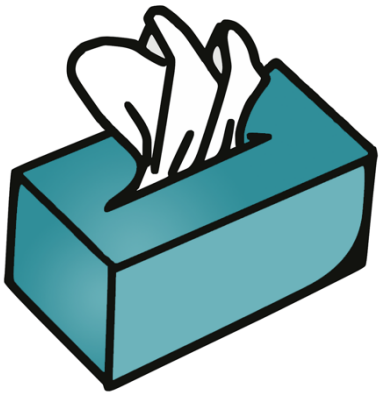
A deficiency in alpha-1 antitrypsin is associated with asthma and allergy exacerbations. Numerous studies have been undertaken investigating the link between these exacerbations and AATD. One such is *Alpha-1 antitrypsin deficiency and Pi*S and Pi*Z SERPINA1 variants are associated with asthma exacerbations,* by Martin-Gonzalez, E., (7). They found a significant association with asthma exacerbations for both Pi*S and Pi*Z (the two variants they studied).



From *The Cost of Care* white paper
https://group.zurich.com.au/content/dam/au-documents/files/advisers/cost-of-care-whitepaper.pdf

Asthma affects people of all ages, but the occurrence

- is more common in women aged over 15 years of age
- increases with decreasing socioeconomic status
- increases with the outer regional and remote areas of Australia (compared with major cities).



The Cost of Care white paper
https://group.zurich.com.au/content/dam/au-documents/files/advisers/cost-of-care-whitepaper.pdf

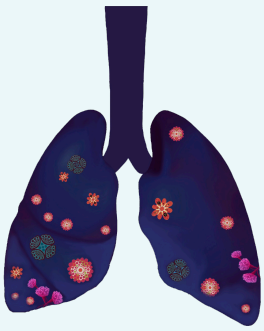
Lung disease contributes more than 10% to the overall health burden of Australia. People with asthma, emphysema or COPD spend an average of $1,642 each year on their out-of-pocket (OOP) healthcare

• Chronic respiratory conditions affect more than a quarter of the population
• It is estimated that there are 2.5 million Australians living with asthma
• Another serious and costly respiratory illness is chronic obstructive pulmonary disease (COPD). COPD is a condition that limits airflow to the lungs and is not fully reversible with the use of medication
• in 2022, around 638,000 people in Australia were estimated to be living with COPD (2.5%) of the population
• There are 19 deaths per day from COPD
• COPD was a leading underlying cause of death in Australia, representing 4.0% of all deaths in 2022
• Three quarters of all COPD cases can be attributed to tobacco
• Its 5-year survival rate can be as low as 40%
• Of Australians with lung disease, COPD contributes to almost one-third of all deaths and costs patients an average of $9,020 in out-of-pocket costs per year.
• 78% of people living with advanced COPD experienced economic hardship from managing their illness and 27% were unable to pay their medical expenses

Cost of respiratory conditions in Australia

Although healthcare in Australia is largely publicly funded, there are still significant OOP costs associated with diagnosis and treatment including:

- GP and specialist gap payments
- Medicines, pharmaceuticals and therapeutic products
- Diagnostic tests outside of public system
- Medical devices and equipment purchase/hire
- Procedures and surgery
- Management of complications and comorbidities
- Travel and accommodation



Atopy

"Atopy is defined as the genetic tendency to develop allergic diseases with a heightened immune response to ingested or inhaled allergens.
A lack of normal AAT activity may potentiate allergic and bronchospastic responses.
Asthma genes may play a role in AATD individuals even without clinical asthma."

The American Academy of Allergy, Asthma & Immunology (AAAAI, 2019) (5)

"The presence of atopy in asthmatic patients with AATD is significantly higher than in asthmatic patients without gene mutation. In addition, a higher percentage of AATD patients self-reported allergic manifestations.

Aiello, M., et al, (1)

AATD, Asthma and Allergies

It is well established that a deficiency of Alpha-1 Antitrypsin (AAT) is associated with an increased propensity to develop asthma and allergies, including allergic rhinitis (hay fever) and urticaria (hives). Numerous studies have been undertaken determining that this is significant.

One of the leading investigators in this field is Edward Eden, along with many co-researchers. An early study establishing this relationship is *Atopy, Asthma, and Emphysema in Patients with Severe ?? -1-Antitrypysin Deficiency* from 1997. They showed that asthma is more common in patients with AATD than in those without it and suggest that a lack of AAT in airways increases the propensity to develop asthma. (3)

Eden undertook a large survey study across a large group of medical centres and laboratories (2) and found that asthma was present in 21% of the cohort with AATD and an elevated level of IgE (associated with allergy) in 17% and this was significantly associated with signs and symptoms of asthma and an allergy history. He concluded that symptoms and signs of asthma are common in AAT deficiency and may start at the age of most rapid FEV1 loss. A further study was carried out in 2006 with Charlie Strange, Brian Holladay, Lianqi Xie (4) to determine the prevalence of asthma and atopy, in a large group of subjects with alpha-1 antitrypsin deficiency (AATD) participating in the Alpha-1 Foundation Research Registry. 44.6% of this group reported MD diagnosed asthma, and wheezing was reported in 76% with respiratory infections, activity and exposure to dusts, fumes, and allergens as common triggers. 83% of those reporting asthma in the PiZZ group also reported a COPD diagnosis.

Eden et al (4) believe that patients with AATD who are susceptible to asthma require allergy evaluation and aggressive anti-inflammatory strategies as part of their management.

Martín-González, E, et al, (7) in 2023 have looked further into these connections finding similar correlations. They say the link between AAT deficiency and asthma might be represented by the elastase/anti-elastase imbalance, but this has yet to be established.

Airway Inflammation

Although less well appreciated than pulmonary emphysema, inflammation of the airways is an early and important finding in alpha-1 antitrypsin deficiency (AATD). The spectrum of clinical presentations of airways disease includes cough and wheezing that is frequently mis-diagnosed as asthma. Study of the airway's inflammation in sputum or the proximal airways usually reveals neutrophilic inflammation (generally from neutrophil elastase). Bronchiectasis is a common finding in areas of pan-lobular emphysema in severely deficient AATD. (Strange, 5)

Asthma sufferer struggling to breathe

Zoom Events / Meetings:

a) Our friendly monthly **support group meetings** are open to everyone diagnosed with Alpha-1. Meetings are held on the third Wednesday of each month at 2pm AEST. If you would like to join in but this time is impossible for you, we'd love to hear from you.
b) On the **4th of October 2024** at 12pm AWST (Perth Time) we are hosting a special meeting for Alpha-1 patients in Western Australia. Our quest speaker Dr Sanjay Ramakrishnan will be speaking about **Alpha-1 clinical trials on offer in Perth**. If attending, please feel free to bring questions along.
c) On 20 November 2024 at our support meeting, we have a special guest speaker from the Lung Foundation discussing **Lung Health - Back to Basics**.

If these meetings are of interest, please email us for the *Zoom links - email pres.a1oa@gmail.com.*

Urticaria (hives) and AATD

Hives (Urticaria) are itchy lumps or spots found on the skin and can range from a rash to blotches and raised welts. They are often caused by an allergic reaction.

This is another condition where a deficiency in alpha-1 antitrypsin has been shown to be a significant contributing factor. See, for example, a study published by Doeglas, H., Klasen, E. and Bleumink, E. in 1985 (9) where MZ and ZZ phenotypes were found to be significantly more frequent in urticaria patients.

Arm with urticaria rash

Back with lumpy welted urticaria

Clinical Trials

To keep up to date with clinical trials in Australia, visit
https://www.australianclinicaltrials.gov.au/

Takeaways from talks presented at 2024 Education Day Alpha-1 Foundation, Salt Lake City, USA & online.

Lung Valves - Gregory A. Grandio, MD, Interventional Pulmonologist, Intermountain Health, Murray, UT

- *Trapped air in the lung affects the diaphragm and makes it less efficient.*
- *The aim is to reduce trapped air in the lungs. Smokers often have air trapped in the top of the lungs. Alphas generally have the lower lobes affected. This can be removed surgically, or valves can be put in place so air can leave but not enter.*
- *In emphysema, air valves help in certain cases but not all. Tests are done to determine whether valves will be beneficial e.g. lung spirometer, 6 min walk test, arterial blood tests, CT scan, perfusion scans. A balloon occlusion test is done under anaesthesia. A balloon is placed where the valve would be inserted and then inflated. If air enters then valves won't work so are not inserted.*
- *If valves are successful the overinflated lungs reduce in size so lobes can inflate more normally, the diaphragm can return to a dome shape, thus working better.*
- *Patients' quality of life is improved post valve placements, although this is not a cure.*

Patient Panel

- *All Alpha-1 patients can produce a short (60 second) statement about Alpha-1 and lobby their elected representatives.*
- *Alpha-1 patients could approach people on oxygen and ask if they had been tested for Alpha-1.*
- *When travelling overseas, Alphas may be affected by headaches, tiredness. Travelling with a portable oxygen concentrator can obviate this.*
- *Having a valve to collapse the lower lobes can allow the upper lobes to inflate properly. One patient gained 14% of lung function and could exercise longer and harder.*
- *A patient's story- speaker was diagnosed with AATD after donating blood to the Red Cross and a researcher tested samples. Later he applied for new health insurance and was found to have liver issues. He suffered from fluid retention that led to breathing issues. A liver biopsy led to a liver transplant which failed but a few days later he received a second liver. This was successful and has lasted for 22 years.*

Alpha-1 Biomarker Consortium Cheryl Pirozzi, MD, MS, Pulmonary and Critical Care Medicine, University of Utah, Salt Lake City, UT

- *Their aim is to work out which Alpha-1 will get worse over time. They hope to find biomarkers to predict this. 271 patients are enrolled in a longitudinal study in 6 US states. Other trials are looking for biomarkers in blood and sputum samples. They also did lung function tests and issued blood spot cards to use at home. 53% were on augmentation therapy at various dose rates. They collected data on smoking & vaping exposure, lung function test results, Covid vaccinations and infections plus out-door pollution exposure.*

References

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4. Eden, E., Strange, C., Holladay, B., Xie, L., *Asthma and allergy in alpha-1 antitrypsin deficiency*, *Respiratory Medicine* Volume 100, Issue 8, August 2006, Pages 1384-1391

5. Strange, C., *Airway Disease in Alpha-1 Antitrypsin Deficiency, Journal of Chronic Obstructive Pulmonary Disease,* Published online: 25 Mar 2013, Pages 68-73

6. *The American Academy of Allergy, Asthma & Immunology (AAAAI, 2019*

7. *The Cost of Care* white paper
https://group.zurich.com.au/content/dam/au-documents/files/advisers/cost-of-care-whitepaper.pdf

8. Martín-González, E., et al, *Alpha-1 antitrypsin deficiency and Pi*S and Pi*Z SERPINA1 variants are associated with asthma exacerbations***,** J Pulmonology, 2023 May 24: S2531-0437(23)00091-0.

9. Doeglas, H., Klasen, E, Bleumink, E. *Alpha-1-antitrypsin-deficiency and PI typing of patients with chronic urticaria***,** *British Journal of Dermatology*, April 1985, 112(4):381-385