alpha-1
ORGANISATION AUSTRALIA INC

Alpha Times

Newsletter of Alpha-1 Organisation Australia inc *Issue 21 Winter 2025*

From the President's Pen

Anyone living with a genetic chronic disease with no government subsided treatment knows how hard it is both emotionally and physically. Those who are lucky enough to participate in an Alpha-1 Antitrypsin Deficiency clinical trial can experience health benefits e.g. slowing down lung and or liver damage or removing the risk of further disease. Current Alpha-1 clinical trials are a blessing in many ways, including the offer of hope to the next wave of Alpha-1 patients. However, the scientific community and patients don't always reflect on the many benefits of functional alpha-1 antitrypsin and its positive impact on various organs. I read recently about the increased risks of skin cancer, leukemia, liver cancer (4), atrial fibrillation and sleep apnea (5) with Alpha-1 Antitrypsin Deficiency. Clearly, accessing treatment has many benefits and I thank everyone who has participated in an Alpha-1 clinical trial and encourage everyone who is eligible to participate to help build a better future for Alpha-1 patients.

Many Alpha-1 patients aren't eligible for clinical trials and need to cope with a myriad of symptoms e.g. difficulty swallowing, shortness of breath, ascites or chronic fatigue. Some argue that we need to remain hopeful, educated, and finds ways to enhance our quality of life. Self-care and embracing small moments, adapting to limitations, connecting with others, practicing mindfulness and using focused breathing are suggested coping strategies. However, recipes for happiness don't work when one has diminished capacity, is experiencing depression, treading water and the external world is becoming smaller. How do we build back a version of what we had? Participating in clinical trials may help, as can acceptance, which allows one to build a bigger internal world filled with things that amaze and interest us. If you have a ´new normal' which is helping you physically or mentally please consider reaching out and sharing your story in a future edition of Alpha Times. We would love to hear and learn from you.

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

Stay away from fires and smoke this winter

The Relationship Between Alpha-1 Antitrypsin and Asthma

Emerging studies suggest a potential link between α1-antitrypsin deficiency (AATD) and asthma, a chronic respiratory condition characterized by airway inflammation and hyper-responsiveness. E.g., Pini et al 2021 (7) and Martin-Gonzalez et al (6).

AATD is a genetically inherited disease with a variable clinical spectrum of lung-related diseases. Pulmonary involvement of AATD may also include emphysema, asthma, and bronchiectasis. Asthma and AATD are mutually exclusive disease entities, but the commonality of neutrophil inflammation across the diseases might suggest common underlying mechanisms of effect.

The diseases share many clinical and functional features: patients with AATD commonly first present with asthma-like symptoms; functional alterations may be common to both, such as bronchial hyperresponsiveness or fixed obstruction after bronchial remodelling. It has been recognized that allergy and asthma often coexist with AATD, but the relationship between allergy, asthma and AATD is not clear.

Genetic Susceptibility

AATD, rooted in mutations in the SERPINA1 gene, may predispose individuals to asthma. While AAT's primary role involves protecting lung tissue from neutrophil elastase, its deficiency could exacerbate airway inflammation, creating conditions favourable for asthma development. As alpha-1 antitrypsin (AAT) is the main inhibitor of the serine proteinase and it is an important anti-inflammatory protein with pronounced immunomodulatory activities, it can be hypothesized that the link between AATD and asthma might be represented by the elastase/anti-elastase imbalance and the proinflammatory effect that occurs because of the reduction of this protein.
The interplay between genetic predispositions, immune responses, and inflammatory mediators lays the foundation for examining the role of AAT in asthma.

Therapeutic Implications

Understanding the relationship between AAT and asthma opens avenues for targeted therapies.

Clinical Evidence and Research

Several clinical studies have aimed to elucidate the link between AAT and asthma. For instance:

- A study examining asthmatic patients with AAT deficiency found that these individuals often exhibited more severe symptoms compared to asthmatics with normal AAT levels.
- Research on paediatric populations has suggested that low AAT levels may be associated with early-onset asthma, indicating a potential role in disease development.
- Animal models have demonstrated that AAT supplementation can mitigate airway inflammation, offering insights into therapeutic possibilities.

While these findings are promising, further large-scale studies are needed to establish definitive causal relationships and refine treatment approaches.

Challenges and Future Directions

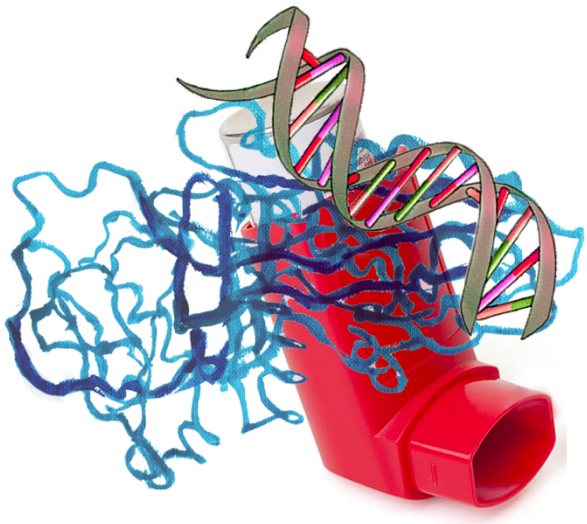
- Limited Awareness: AAT deficiency is underdiagnosed, with many individuals unaware of their genetic predisposition.
- Complex Interactions: The multifactorial nature of asthma complicates efforts to isolate the impact of AAT levels.

Future research should focus on:

- Large-scale epidemiological studies to determine the prevalence of asthma in individuals with AAT deficiency.
- Exploring the efficacy of AAT augmentation therapy as well as emerging therapies in asthma management.
- Investigating the molecular mechanisms underlying the relationship between AAT and airway inflammation.

Conclusion

There is a need for further research to better understand the molecular mechanisms binding AATD and asthma. While AAT deficiency is well-established as a risk factor for conditions like emphysema, its role in asthma remains a subject of ongoing research. Understanding this connection could lead to improved diagnostic tools, personalized treatment strategies, and better outcomes for individuals with asthma and related respiratory conditions.



Inhaler entangled with DNA strand and AAT molecule

COPD and Difficulties with Swallowing (Dysphagia)

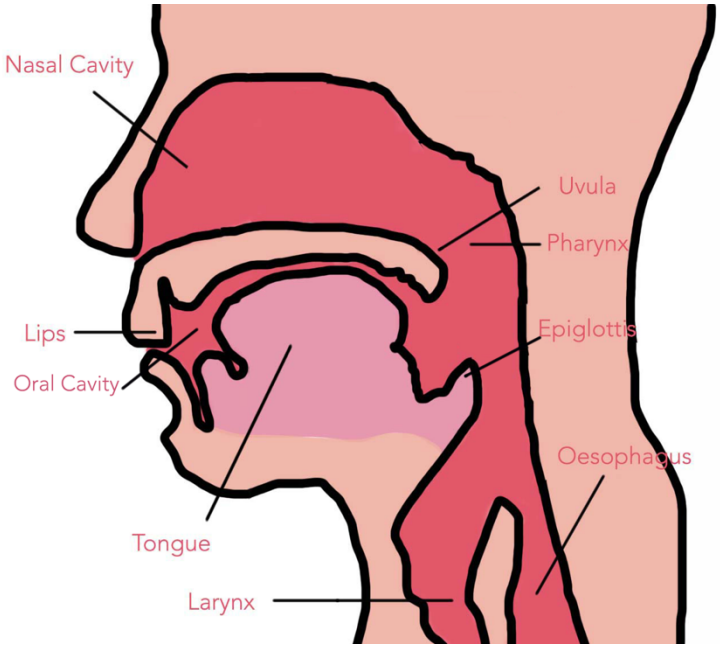
It is well known that Alpha-1 patients are at higher risk of COPD, especially those with the PiZZ phenotype. COPD is associated with dysphagia (difficulty swallowing). This can occur as the upper airway serves the dual functions of breathing and swallowing. With COPD e.g. emphysema, chronic bronchitis, there may be a disrupted coordination of the breathing cycle, cricopharyngeal muscle dysfunction (located at the junction of the pharynx and oesophagus) or changes in lung volume, leading to problems with swallowing. Disrupted breathing / swallowing coordination puts COPD patients at risk of lung aspiration (breathing in food, liquids, foreign material into the lungs) which can cause many problems including pneumonia / exacerbations and lung damage. An acute lung exacerbation is associated with a higher risk of aspiration (evident in at least 33% of COPD patients).

Other issues have been reported to impact the passageway for food and air (the laryngopharynx) e.g. airway inflammation, reflux and some medications - inhalers with anticholinergic agents and antihistamines and dyspnoea (shortness of breath). These issues are associated with aspiration risk. While there appears to be a need for further dysphagia research and management strategies, several have been suggested including:

- Limiting distractions when eating and drinking - focusing, pausing and eating and drinking slowly.
- Eating small pieces of food (avoiding big bites) and having smaller more frequent meals.
- Tucking the chin towards the chest when swallowing to help close the airway and allow food / drink to travel to your stomach.
- Thickening drinks with a special thickener to help them move more slowly and stay in the right passage.
- Double swallowing (dry swallows).
- Addressing reflux.

It has also been suggested that pharmacological agents, such as angiotensive-converting enzyme (ACE) inhibitors may have some protection benefits but more research is needed.

See Cvejic (2), Zheng (10), and Gross (3) below.



New treatment for Asthma - Biologics

What are biologic treatments?

Biologic drugs (biologics) are a kind of medicine that has a biological origin, they are made by living things, such as animals, plants, or bacteria. These are monoclonal antibodies (molecules produced in laboratories engineered to serve as substitutes for antibodies). They are used to block, enhance or modify the body's immune response. Asthma biologics work by disrupting cells or blocking specific molecules that trigger inflammation.

What is asthma?

Asthma is a multifactorial condition influenced by genetic, environmental, and immunological factors. It is characterized by chronic inflammation of the airways, bronchial hyper-reactivity, and episodic obstruction, which manifests as wheezing, coughing, shortness of breath, and chest tightness. The inflammation in asthma is driven by immune cells such as eosinophils, mast cells, and T-helper type 2 cells, which release cytokines that exacerbate the condition.

How is asthma treated?

These common asthma symptoms are usually treated with inhaled medicine and/or pills.
If you have moderate-to-severe asthma, you may have to take routine asthma controller medicine to decrease the swelling in your airways. Sometimes, these medicines are not enough to manage your symptoms. If your routine medicines are not working well on their own, an add-on controller therapy called a biologic might be an option for you.

How do biologics treat asthma?

Biologics work by disrupting specific cells or blocking specific molecules in your immune system that make your airways swell after exposure to certain triggers.
Different sets of molecules are responsible for certain types of immune reactions. There are different biologics to target different types of asthma responses.

What asthma biologics are available in Australia?

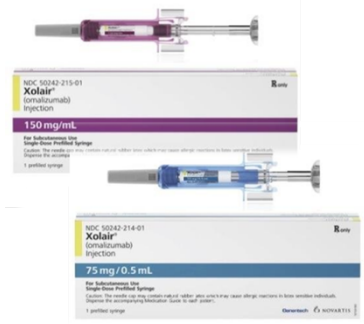
In Australia there are five biologics available. These are benralizumab (Fasenra), dupilumab (Dupixent), mepolizumab (Nucala), omalizumab (Xolair), and dupilumab (Dupixent). These are administered by injection at different intervals, depending on the particular drug, usually every 2 or 4 weeks. Your specialist will determine which biologic is right for you if it is established that you need it for your asthma.

Efficacy

Alpha-1 patients are reporting an improvement in asthma symptoms with the use of biologics, although some have experienced side effects such as a localised allergic reaction.

A good overview of the different asthma biologics can be found at

https://www.meded101.com/biologics-in-asthma-the-basics/



Xolair injections

Alpha-1 Foundation 10th Patient Congress

April 5, 2025, Lisbon, Portugal

Bringing together global experts, researchers, industry leaders, and patients and families affected by AATD. The energy in the room was electric, with a strong sense of shared purpose: to drive meaningful progress and improve lives.

1. Patients Are at the Heart of Progress

Scott Santarella, CEO of the Alpha-1 Foundation, opened the Congress by reminding everyone that patients aren't just participants—they're partners in research and advocacy. Your voice, your experience, and your involvement are critical to advancing treatment and shaping healthcare policy.

2. Cutting-Edge Gene Editing Shows Promising Results

One of the most exciting updates came from Beam Therapeutics, who shared early results from their BEAM-302 base editing trial—a potential one-time gene editing therapy for AATD.

At 28 days after a single dose, participants showed a 91% increase in corrected M-AAT protein and a 79% decrease in the harmful Z-AAT protein.

A higher 75mg dose is now being tested, with more results expected later this year.

This is one of the most advanced gene-editing trials for Alpha-1. If successful, this could be a disease-modifying therapy—possibly reducing or eliminating the need for lifelong augmentation.

3. Inhaled Therapy on the Horizon

Kamada's inhaled AAT therapy is currently in clinical trials. This targeted treatment aims to deliver the therapy directly to the lungs where Alpha-1 causes the most harm. Early results suggest it's safe and potentially very effective.

This offers an accessible and focused treatment, especially for those who can't access or tolerate regular infusions.

4. The Power of Patient Registries

A panel of leading researchers underscored how patient registries and clinical trial participation are essential. Registries help researchers understand patterns, track outcomes, and match people to new trials. Global efforts like EARCO and the Alpha-1 Foundation are making it easier to connect patients with opportunities.

Whilst there is no dedicated AATD registry in Australia, there are efforts to establish one. It's one of the most powerful ways to drive progress through data. Stay in touch with us for updates.

5. Augmentation Therapy: Challenges and Victories

International leaders from Canada and Europe shared hard-won lessons in making augmentation therapy available and reimbursed. They found that policy and advocacy were key to success.

Patient organisations like ours, Alpha-1 Organisation Australia, play a central role in making change happen. Strong voices from patients in Australia will be vital as we push for expanded access and innovation.

6. Global Industry Support Is Stronger Than Ever

CSL, Grifols, and other sponsors reaffirmed their ongoing investment in Alpha-1 research, safety improvements, and support for the global Alpha-1 community. With these and other companies committed to innovation there's more momentum and competition, both of which drive faster breakthroughs.

7. Spotlight on South America

Dr. Mariano Fernandez Acquier highlighted efforts in South America to improve diagnosis rates, set up registries, and build support networks—despite limited access to therapy.

The Alpha-1 community is growing stronger globally. Australia has the chance to be part of this change by standing with others and sharing what works.

How Can You Help Keep the Momentum Going?

- Share your story—your lived experience helps researchers, policymakers, and new patients understand the real impact of Alpha-1. (Contact us if you'd like to find out more on how to share your story).

- Follow the science—stay up to date with us through newsletters and webinars.

- Support research by encouraging participation in trials or donating if you're able.

Together, we can make Australia a key voice in global Alpha-1 advocacy.

The future for Alpha-1 patients is changing rapidly—and your voice matters more than ever.

Zoom Events / Meetings:

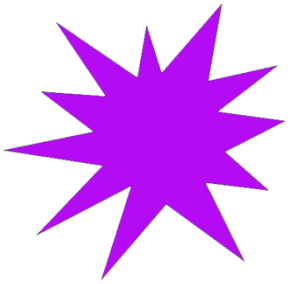
Our friendly monthly **support group meetings** are open to everyone diagnosed with Alpha-1 and anyone with a family member affected by Alpha-1.

Meetings are held on the third Wednesday of each month at 3pm AEST. If you would like to join in but this time is impossible for you, we'd love to hear from you.

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

Clinical Trials

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



2025 AGM
11 August, 7pm AEST
Board nomination details will be emailed to financial members a few weeks prior.

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