ORGANISATION AUSTRALIA INC

Alpha Times

Newsletter of Alpha-1 Organisation Australia inc *Issue 15 Summer 2023/24*

From the President's Pen

Hi everyone,
Welcome to our Summer Edition and our first 2024 newsletter! I hope that you had a pleasant festive season and that 2024 has commenced well.

February is always an important month on the rare disease calendar. As a leap year, this year rare disease day falls on Thursday 29 February. At Alpha-1 Organisation Australia we embrace international rare disease day as an opportunity to raise awareness of Alpha-1 Antitrypsin Deficiency (Alpha-1) and diseases associated with this genetic disorder.
We encourage everyone associated with the Alpha-1 community to take the opportunity and raise awareness of Alpha-1 on rare disease day! This can occur in many ways including sharing information about Alpha-1 including links to our charity's YouTube channel –https://www.youtube.com/@alpha-1organisationaustral421 – where a new video on Alpha-1 will be released during February as part of our "Alpha-1 Unwrapped" video series. Our latest videos will feature health professionals that Alpha-1 patients encounter, demystifying issues associated with an Alpha-1 diagnosis and ongoing management.
Our friendly monthly Alpha-1 patient support meetings commence on 21 February – meeting via Zoom. The meetings provide support to anyone diagnosed with Alpha-1 and occur at 2pm on the third Wednesday of the month - NSW time. Please reach out for Zoom meeting details at contactus.a1oa@gmail.com. I aim to attend most meetings this year and I will be hosting some. If you would like to join as a ***guest host***, please let me know. I would love to hear from potential ***guest speakers*** too who could speak for 10 – 30 minutes on any topic related to Alpha-1. This allows up to 30 minutes for questions and general discussion, as support meetings run for around one hour.
I am looking forward to a wonderful year with so many Alpha-1 clinical trials being offered in Australia which are needed and appreciated by our community.

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

COPD and Alpha-1

According to the World Health Organisation, Chronic Obstructive Pulmonary disease (COPD) is the third leading cause of death worldwide.

COPD is a common lung disease causing restricted airflow and breathing problems. It is sometimes called emphysema or chronic bronchitis.

In people with COPD, the lungs can get damaged or clogged with phlegm. Symptoms include cough, sometimes with phlegm, difficulty breathing, wheezing and tiredness.

As medical professionals and Alphas who are lung affected know, these symptoms of COPD are common in the Alpha-1 community. We struggle with breathing, chronic cough (usually with phlegm) and feeling tired.

COPD symptoms can get worse quickly. These are called flare-ups or exacerbations. These usually last for a few days and often require additional medicine.

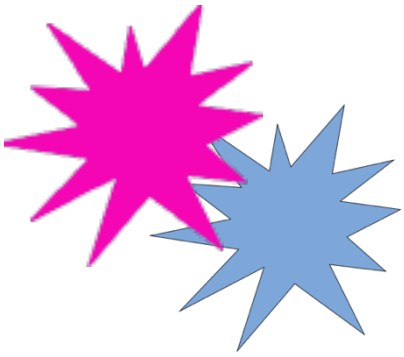
People with COPD also have a higher risk for other health problems. These include:

- lung infections, like influenza or pneumonia
- lung cancer
- heart problems
- weak muscles and brittle bones
- depression and anxiety.

COPD symptoms usually start in mid-life as damage is cumulative and worsens over time.

References
https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

https://www.who.int/news/item/15-11-2023-smoking-is-the-leading-cause-of-chronic-obstructive-pulmonary-disease#:~:text=%E2%80%9CAs%20well%20as%20being%20a,companies%20actively%20seek%20new%20customers.



Rare Diseases Day
29 February

Tell your friends about Alpha-1!

Tell everyone!

COPD and Lung Hyperinflation

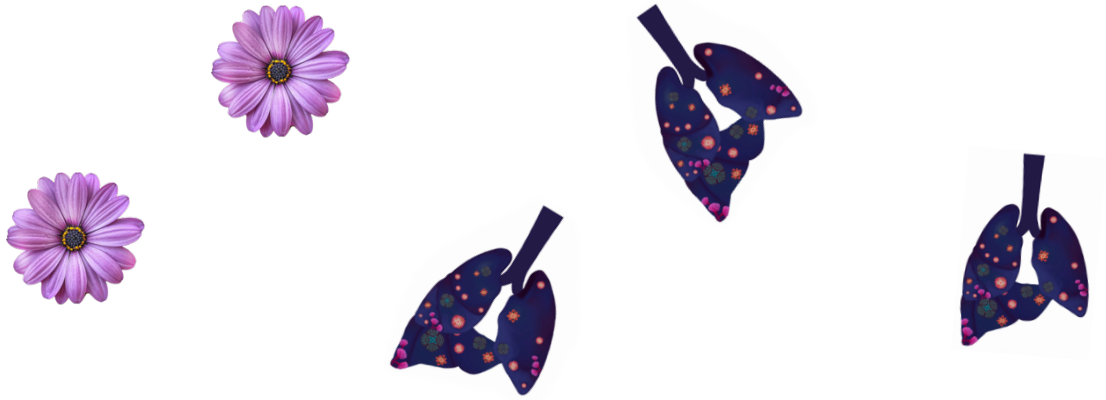
COPD is a complex condition with a variety of factors contributing to its pathophysiology with the importance of these factors varying between patients. The name, COPD, refers to the two conditions, chronic bronchitis and emphysema. The former is characterised by obstruction of airways resulting from inflammation and changes in the larger airways, with oedema and increased mucous production and the latter by irreversible damage to the lung parenchyma (lung parenchyma is comprised of a large number of thin-walled alveoli, forming a large surface area, which serves to maintain proper gas exchange) and adjacent vasculature.

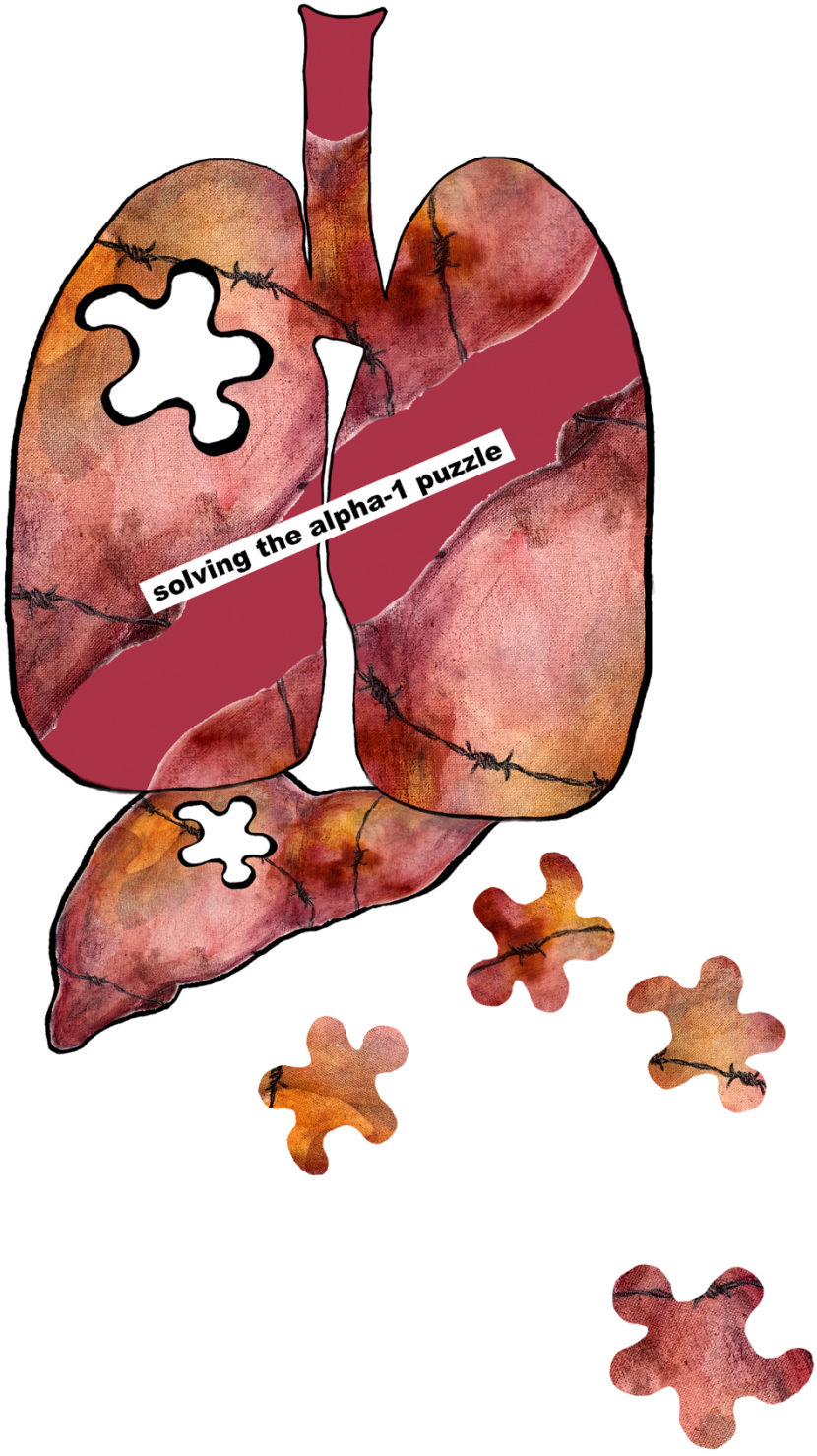
It is estimated that chronic obstructive pulmonary disease COPD affects 40% of people over 40 years of age. Sufferers are progressively limited in their ability to exercise and undertake daily activities. This is due to a combination of exertional dyspnoea (shortness of breath) and peripheral muscle weakness. COPD is characterised by limitation in expired air flow, which results in air being trapped in the lungs causing hyperinflation of the lungs. This increases during exercise or exacerbations, usually resulting in reduction of and avoidance of physical activity by the affected individual, leading inevitably to lower fitness levels, reduced quality of life and potential development of comorbidities like cardiovascular disease.

Strategies to prevent hyperinflation include use of long-acting bronchodilator medications ("puffers") and exercise programs.

Reference:

Thomas, M., O'Donnell, Decramer & Denis E., *No room to breathe: the importance of lung hyperinflation in COPD.*
Primary Care Respiratory Journal volume 22, pages101–111 (2013), 21 February 2013
https://www.nature.com/articles/pcrj201325





Alpha-1 Organisation Australia (A1OA) is advocating for Alphas, raising awareness by establishing relationships with research companies and professors, government agencies, and doctors and clinicians, publishing resources such as information brochures for doctors and patients as well as fun designs for t-shirts and tote bags, and providing services such as Mental Health First Aider.

Summary of AATD (and its Prevalence in Sweden)

In Sweden, the prevalence of alpha-1 antitrypsin deficiency (AATD), is 1/1600, established by a nationwide screening program of all 200,000 newborns over the period 1972-1974, with 127 homozygotes identified (referring to individuals who have inherited two identical copies of a gene, i.e., one from each parent, e.g., ZZ, SS).

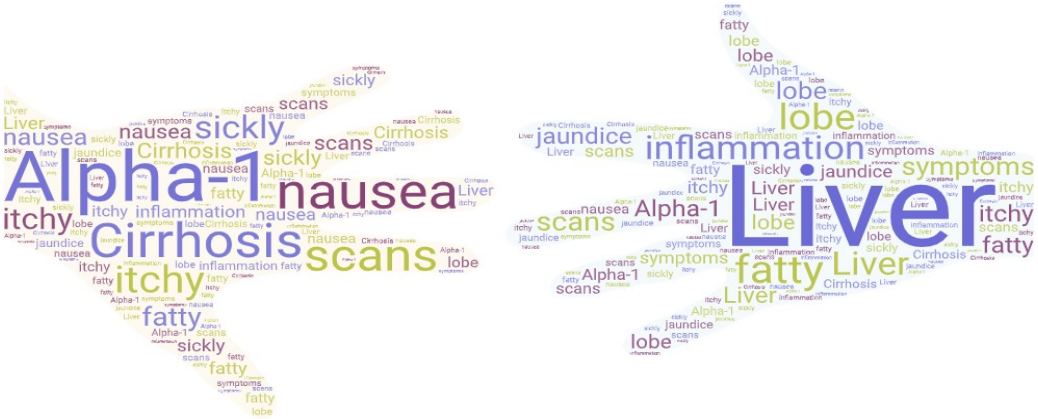
Severe alpha-1 antitrypsin deficiency piZZ, is an autosomal, codominant, hereditary disorder characterized by low levels of AAT in serum and lungs in the affected individual. The main function of AAT is to inhibit neutrophil elastase and other serine proteases.

This genetic defect results in the polymerization of the AAT molecule in the hepatocytes (cells within the liver), leading to an accumulation of the Z protein within the hepatocytes,
and a decreased release into the circulation. AATD contributes to protein degradation and increased inflammation because of pro-inflammatory effects of polymerized AAT and the loss of anti-inflammatory and antiproteolytic functions.

Major causes of disability and death associated with severe AATD are early-onset panacinar emphysema (characterised by permanent destruction of the airspaces, i.e., alveoli, distal to the respiratory bronchioles) and liver disease, which typically presents as cholestasis in infancy, and cirrhosis and primary liver carcinoma in adulthood. Patients also report suffering from systemic vasculitis, necrotising panniculitis and other inflammatory and neoplastic diseases (causing tumour growth).
(Cholestasis is a slowing or stalling of bile through the biliary system. It can be a problem in the liver or in the bile ducts. Bile that can't flow leaks into the bloodstream and backs up into other organs, causing inflammation. Bile that can't reach the intestines can cause digestive problems.)

Information taken from
https://www.tandfonline.com/action/doSearch?AllField=Hanan+A+Tanas%2C+Magnus+Ekstr%C3%B6m%2C+Philippe+Wagner%2C+Eeva+Piitulainen%2C&SeriesKey=dcop20

Reference:
Hanan A Tanas, Magnus Ekström, Philippe Wagner, Eeva Piitulainen, *Cause-specific mortality in individuals with severe alpha 1-antitrypsin deficiency in comparison with the general population in Sweden,* Published online: 27 Oct 2022.



Cause-specific mortality in individuals with severe alpha 1-antitrypsin deficiency in comparison with the general population in Sweden.

This study was undertaken since while it is known that Severe alpha 1-antitrypsin deficiency (PiZZ) predisposes to morbidity and mortality due to early-onset emphysema and liver disease the risk of death from other causes, including cardiovascular disease (CVD) and cancer, has not been well investigated.

The authors analysed cause-specific mortality in PiZZ individuals compared with the general Swedish population. PiZZ individuals had excess all-cause mortality compared with the Swedish general population. The median follow-up period was 12 years, and no patient was lost to follow-up.

The causes of death were available for all decedents. The main causes of death were COPD and its complications such as respiratory failure and infections (54%), liver diseases (14%), CVD (15%), and cancer (17%).

PiZZ patients had significantly increased mortality due to respiratory and hepatic diseases, pulmonary embolism, and colon diverticulitis compared with the general Swedish Population.

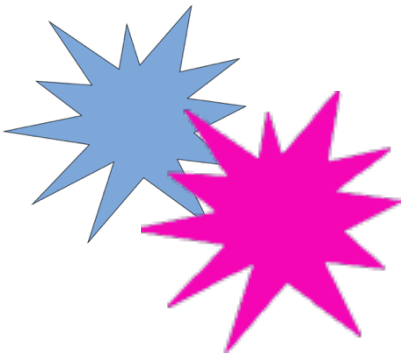
In contrast, they had a reduced risk of mortality due to IHD (ischemic heart disease), and no increased mortality risk due to CVD as a whole. However, mortality due to heart failure was significantly increased. Of the 18 patients who died of heart failure, eleven had COPD, one had pulmonary fibrosis, and one had Marfan's syndrome. Complicated colon diverticulitis with peritonitis was the cause of death of five patients; none of these patients had known inflammatory bowel disease. Read an article on AATD as possible risk factor for colonic diverticulitis here: https://pubmed.ncbi.nlm.nih.gov/32666625/#:~:text=Aim%3A%20Connective%20tissue%20changes%20due,in%20the%20aetiology%20of%20diverticulosis.

PiZZ individuals had increased mortality compared with the general population for the following diseases: respiratory disease, primary liver carcinoma, complicated colon diverticulitis, and pulmonary embolism.

Smoking-related differences in mortality
During the follow-up period, 350 ever-smokers and 174 never-smokers died. The mean age at death was lower in ever smokers (65 years) compared with never-smokers (74 years).
For IHD mortality rate was similar for never and ever-smokers, and in males and females.

Conclusion
PiZZ individuals had a reduced mortality risk of IHD. Mortality due to respiratory, hepatic disease, diverticulitis, and pulmonary embolism was markedly increased compared with the age- and sex-matched Swedish population.

Reference:
Hanan A Tanas, Magnus Ekström, Philippe Wagner, Eeva Piitulainen, *Cause-specific mortality in individuals with severe alpha 1-antitrypsin deficiency in comparison with the general population in Sweden,* Published online: 27 Oct 2022.
https://www.tandfonline.com/action/doSearch?AllField=Hanan+A+Tanas%2C+Magnus+Ekstr%C3%B6m%2C+Philippe+Wagner%2C+Eeva+Piitulainen%2C&SeriesKey=dcop20



Don't forget to check the A1OA YouTube channel for useful video resources.

https://www.youtube.com/@alpha-1organisationaustral421

Alcohol consumption can negatively affect COPD by worsening lung function, causing allergic reactions and creating difficulty breathing during sleep.

Alcohol affects every function and system of the body, regardless of whether a person has COPD. Alcohol use can exacerbate COPD symptoms and can affect:

- Lung health
- Sleep quality
- Allergic reactions

Drinking high quantities of alcohol can harm healthy lung functioning and thereby worsen COPD. Over time, drinking too much alcohol can weaken the lungs' ability to clear themselves of mucus. This issue can lead to breathing problems and symptom exacerbation in people with COPD.

https://www.therecoveryvillage.com/alcohol-abuse/does-alcohol-affect-copd/#:~:text=Drinking%20high%20quantities%20of%20alcohol,exacerbation%20in%20people%20with%20COPD.

Effects of Drinking Alcohol With COPD

Alcohol exposure is associated with increased lung infections and decreased mucociliary clearance. (2) Activation of protein kinase C, elevated lavage fluid cytokines/chemokines including interleukin-6 (IL-6), and the development of significant lung pathology have been observed. (2) Because alcohol blocks airway epithelial cell release of IL-6 in vitro, it was hypothesized by McCaskill et al (2017) that alcohol exposure would alter mouse lung inflammatory responses to dust. They concluded from their data that alcohol is important to consider in the study of inhalation injury responses. By extrapolating from these mouse studies to humans, it can be inferred that consumption of alcohol could contribute to worsening of breathing problems.

Alcohol moves easily from bronchial circulation, across the airway epithelium and into the lungs' conducting airways due to the alcohol's volatility, accounting for many of the biologic effects of alcohol on lung airway functions. (3) Effects would be proportional to exposure.

Additional mechanisms that mediate alcohol effects in the lungs include calcium, nitric oxide, alcohol- and acetaldehyde-metabolizing enzymes such as aldehyde dehydrogenase 2 (3).

References

1. Elsevier Masson, 2018, https://pubmed.ncbi.nlm.nih.gov/29941207/
2. Michael L McCaskill , Debra J Romberger, Jane DeVasure, Jessica Boten, Joseph H Sisson, Kristina L Bailey, Jill A Poole, Todd A Wyatt, Alcohol exposure alters mouse lung inflammation in response to inhaled dust, https://pubmed.ncbi.nlm.nih.gov/22852058/
3. Joseph H Sisson, Alcohol and airways function in health and disease, 2017, https://pubmed.ncbi.nlm.nih.gov/17764883/
4. https://www.therecoveryvillage.com/alcohol-abuse/does-alcohol-affect-copd/#:~:text=Drinking%20high%20quantities%20of%20alcohol,exacerbation%20in%20people%20with%20COPD

Aunty Alpha

Dear Aunty Alpha,
I've read that drinking alcohol can be detrimental to COPD. I'm a ZZ alpha with emphysema and I'm a moderate drinker. Is this something I should be worried about?
Regards
Fred

Dear Fred,
There are numerous articles studying the effects of alcohol on lungs. These indicate that alcohol exposure is associated with increased lung infections and decreased ability to clear mucous. Some information is provided in the articles above from which it can be inferred that consumption of alcohol could contribute to worsening of breathing problems.

I would therefore suggest that alcohol should be consumed in moderation and possibly you should look at reducing your intake. If you are concerned it would be a good idea to talk to your primary care physician and your lung specialist.

Regards
Aunty

If you have a question about anything raised in this issue

write to Aunty Alpha, who is always happy to answer your questions, or contact the A1OA through contactus.a1oa@gmail.com

Alpha-1 Liver Alphabet

A Acute, Alpha-1, anti-inflammatory, alcohol, ascites
B Bile
C Cirrhosis, Cancer
D Diagnosis
E Enzymes, exercise, encephalopathy
F Fatty liver, fibroscan, fibrosis
G Gall bladder
H Health, hepatic, hepatocyte
I Itchy, inflammation
J Jaundice
K Ketosis (keto diet has the potential to be anti-inflammatory)
L Liver, lobe, lesions, loss of appetite, lobular inflammation
M metastases
N Nausea, non-alcoholic fatty liver, normal
O Organ, organoids
P Pain, portal hypertension
R Reflux
S Scans, steatotic liver disease, swelling, scar tissue, serine protease inhibitor
T Transplant
U Urine test (cirrhosis), ultrasound
V Vitamins, varices
W Weighs 1.5kg
X-ray
Y Yellow (jaundice)
ZZ allele