Title: The Evolution of Alpha 1-antitrypsin Deficiency by Kamyar Afshar, DO

- Alpha 1-antitrypsin deficiency should always be ruled out in obstructive lung diseases
- Confirmation testing should be based on the phenotype AND serum values
- Patients with alpha 1-antitrypsin deficiency will need liver function surveillance (LFTs every 6 months and ultrasound annually) and immunization against hepatitis A and B
- Exogenous replacement of the protease inhibitor (“augmentation therapy”) is an additional therapeutic option in individuals with obstructive lung disease confirmed to have alpha 1-antitrypsin deficiency

Chronic obstructive pulmonary disease (COPD) is a common pulmonary disorder with a high prevalence. Smoking history has been considered the predominant factor to developing COPD. Alpha 1-antitrypsin deficiency (A1ATD) continues to be an underappreciated contributing factor for the development of COPD, even though 3-4% of people with COPD have been confirmed to have A1ATD [1]. Reasons for this include, biases that individuals with A1ATD are young non-smokers with bibasilar disease. Since this is a rare phenomenon there is either lack of testing or misinterpretation of testing results.

More recent observational studies highlight that COPD is not the only clinical feature for individuals with confirmed alpha 1-antitrypsin deficiency. Evidence shows that pulmonary manifestations in A1ATD include asthma, chronic bronchitis, emphysema and bronchiectasis [2, 3]. Hence, clinicians following the ATS guidelines should recommend testing to uncover this genetic deficiency. The ATS recommends testing 1) all adults with symptomatic COPD, regardless of smoking history; 2) all adults with symptomatic asthma whose airflow obstruction is incompletely reversible after bronchodilator therapy 3) adults with bronchiectasis without evident etiology 4) asymptomatic patients with persistent obstruction on pulmonary function tests with identifiable risk factors and 5) test siblings of individuals with alpha 1-antitrypsin deficiency [4]. Health care providers should also be aware that A1ATD is not only found in Whites, but also Hispanics and Blacks [5].

There is an evolution in the understanding of A1ATD. The “deficiency” in alpha 1-antitrypsin deficiency may be a misnomer in certain patients. Having the following phenotypes PiSZ, PiZZ or Pi Null are considered the “deficiency” alleles. The deficiency in alpha 1-antitrypsin deficiency is not only the serum value, but the functionality of the proteins available. Hence, individuals with Pi-MZ or those with the F or I alleles may have normal serum values, but they are dysfunctional and may warrant augmentation therapy to stabilize lung functions as in patients with confirmed PiSZ, PiZZ or Pi Null [6]. Being vigilant in making this diagnosis has clear implications in natural history of lung function decline and thereby patient survival. To offset the rapid decline in the lung functions, individuals with A1ATD may benefit from augmentation therapy. Patients with A1ATD may also need surveillance for liver disease that is usually not considered in general COPD guidelines.
Reference: