South West Primary Care referral and advice pathway for patients and family members with or at risk of developing Alpha-1 Antitrypsin Deficiency (AATD)

University Hospitals Bristol NHS Foundation Trust

AATD is an autosomal recessive disorder affecting about 1:2500 people. It may manifest with emphysema in the third to fourth decades of life. Less frequently, liver disease may arise and cause cirrhosis and liver failure in children or adults. Environmental factors, particularly cigarette smoking, increase the risk of emphysema at an earlier age. Most carriers for AATD are unaffected, but their risk of emphysema is also exacerbated by smoking. Most individuals can be managed in primary care with lifestyle advice, but if significant symptoms arise referral to specialist services may be required.

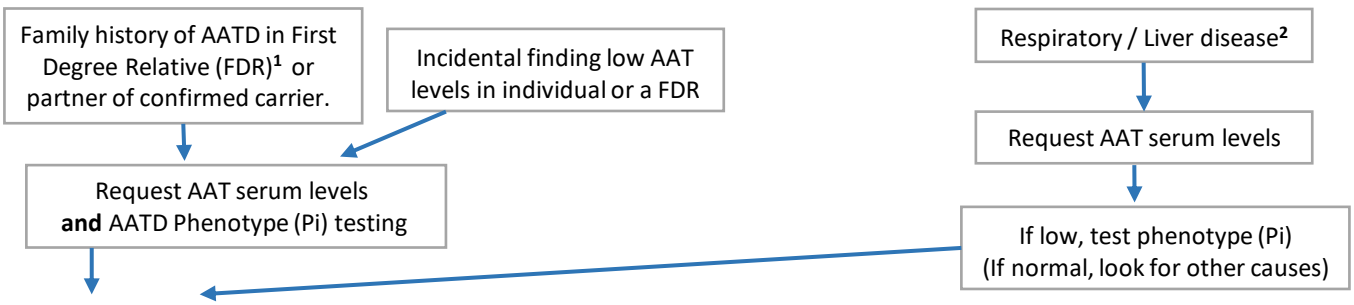
The *SERPINA1* gene produces Alpha-1 Antitrypsin (AAT), a protein that protects tissues from proteolytic damage, in several different forms called alleles. Every individual has two alleles, inheriting one from each parent. The three main alleles of AAT are M, S and Z. M is the most common and associated with normal AAT levels. Z and S are alleles associated with lower AAT levels. S causes moderately reduced but sufficient AAT levels, whereas Z causes very low AAT levels associated with deficiency. Individuals with one M allele and another abnormal allele (S or Z) are called 'carriers'.

Blood Sciences test and sample requirements:

- Serum AAT level AND phenotype → clotted blood sample (gold-top tube) to local blood sciences laboratory

This will report both AAT level and phenotype (allele e.g MM, MZ, ZZ)

Genetic testing can be carried out in primary care if advised by laboratory following initial testing of AAT levels and phenotyping. **Bristol clinical genetics will accept referrals for parents of a diagnosed child, or a couple who are both carriers of abnormal alleles.**



Phenotype (Pi)	Individuals risk of AATD	Management	Family Recommendations
MM	No risk	Reassurance, routine lifestyle advice.	None required.
MS SS	No risk	Reassurance, lifestyle advice regarding smoking and alcohol.	• Provide patient/family information leaflet. • FDRs can seek advice from own GP for phenotype and levels testing. • If planning pregnancy, phenotype partner. • If partner also has abnormal allele(s) refer to Clinical Genetics Service for genetic counselling.
MZ	Slight risk	• Lifestyle advice regarding smoking and alcohol. • Refer to relevant specialist* if symptoms.	
SZ	Increased risk	• Refer to relevant specialist*. • Lifestyle advice regarding smoking and alcohol, including smoking cessation referral.	
ZZ	Significant risk		
Any phenotype where AAT level is undetectable**	Significant risk		
Other reported phenotypes including rare alleles.	Varies.	Will depend on combination, may seek specialist advice.	

* **Relevant specialist = Respiratory, Hepatology or Paediatrics**.

** If a patient has low levels of AAT and may have other rare alleles, genetic testing of the *SERPIN1A* gene can be considered based on criteria in the National Genomic Test Directory.

1 FDR = First Degree Relative: Parent, child or sibling. If an affected individual is not a FDR, then reassure as low risk without testing.

2 European Respiratory Society recommendations are that all COPD patients; all nonresponsive asthmatic adults/adolescents; all people with cryptogenic cirrhosis/liver disease; granulomatosis with polyangitis; bronchiectasis of unknown aetiology; panniculitis have AAT levels tested; however, this is not being done UK-wide.