Understanding Your Alpha-1 Test Results

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Testing for alpha-1 antitrypsin (AAT) deficiency can involve several different types of tests.

Genotyping

- ✓ Genotyping looks at the DNA code for alpha-1 antitrypsin (AAT) in your cells. A sample of DNA is typically taken from blood, inside the cheek, or saliva.
- ✓ Targeted genotyping is the most common type of genotyping. It detects between 2 and 26 of the most common variants, depending on the laboratory. Whole genome sequencing may be necessary to detect rare variants.
- ✓ Genotype is represented as two letters, such as MM, MZ, MS, or ZZ.

Phenotyping

- ✓ An older technology, phenotyping identifies which AAT proteins are present in a blood sample. These proteins are the physical expression of your genes. Very few labs perform phenotyping today.
- ✓ Phenotyping can identify common and rare variants. However, phenotyping cannot identify "null" variants and it is unreliable for individuals who are on augmentation therapy.
- ✓ Results often include "Pi". For example: PiMM, PiMZ, PiMS, or PiZZ. Genotype and phenotype should match. For example, the SZ genotype should lead to a phenotype test result of PiSZ.

AAT Blood Level

- ✓ A blood level measures the amount of AAT protein in a blood sample.
- ✓ Results are expressed either in mg/dL (milligrams per deciliter) or in µM (micromoles).
  - ❑ Interpreting results in mg/dL: The low end of the normal range is approximately 100 mg/dL. Individuals with a level less than 57 mg/dL are considered to have severe AAT deficiency. Levels between 57 and 100 mg/dl are said to have an intermediate deficiency.
  - ❑ Interpreting results in µM: The low end of the normal range is approximately 20 µM. Individuals with a level less than 11 µM are considered to have severe AAT deficiency. Levels between 11 and 20 µM are said to have an intermediate deficiency.
- ✓ AAT blood levels can rise significantly when the body is stressed, such as during an infection or injury. This can happen even in individuals with AAT deficiency, which can make it harder to identify AAT deficiency when using a blood level.
- ✓ Blood level is linked to genotype. Genotypes that are considered severely deficient (such as ZZ) lead to a lower blood level than genotypes that are not deficient (such as MM).
- ✓ Blood levels are a cost-effective screening tool for AAT deficiency. Yet, blood testing can fail to identify intermediate AAT deficiency and this test cannot identify an individual's genotype.
- ✓ Blood levels change every day. For this reason, a decline in blood level should not be used to decide when to start augmentation therapy.
- ✓ It is the opinion of the Medical Directors of AlphaNet that, for individuals on augmentation therapy, it is not necessary to follow blood levels. It also is not advisable to adjust dose or discontinue augmentation therapy based on blood levels. The important level of AAT is the level in the lungs. Research shows that a dose of 60 mg/kg/week provides stable, adequate levels of AAT in the lungs, even when blood levels vary greatly.

Diagnosing Alpha-1 Antitrypsin Deficiency

- ✓ Blood level testing is recommended as a screening tool. If blood levels are low or if AAT deficiency is clinically suspected, genotyping (or phenotyping) should be done to identify specific AAT genes.
- ✓ Once AAT deficiency has been accurately diagnosed, additional testing is not needed. Genes don't change. Augmentation therapy and liver transplantation can change your blood level and phenotype. Your genotype is not changed by augmentation therapy.

Additional Information

- ✓ AlphaNet's Big Fat Reference Guide (BFRG) has more detailed information about AATD test results (especially in Chapter 1). AlphaNet Subscribers can access the BFRG through their Subscriber Portal.
- ✓ The Alpha-1 Alleles website allows you to enter your genotype and learn about the risk for lung and liver disease associated with your genotype.