ALPHA 1 ANTITRYPSIN DEFICIENCY (AAT)

INFORMATION LEAFLET FOR PATIENTS

WHAT IS ALPHA 1 ANTITRYPSIN (AAT)?

Alpha 1 antitrypsin (AAT) is a protective protein that helps protect our organs from being damaged by the body's own enzymes.

WHAT IS AAT DEFICIENCY?

AAT deficiency is an inherited disease caused by low protective levels of AAT. People who have AAT deficiency do not produce enough AAT. This may eventually lead to lung damage and breathing difficulties (chronic obstructive pulmonary disease or COPD). The commonest symptoms of AAT deficiency caused by COPD are shortness of breath, cough and wheeze. People with AAT deficiency who smoke risk developing more severe lung disease than those who are non-smokers and often at a younger age. A small number of people with AAT deficiency have liver problems, either as young children or later in life. These liver problems may be mild but can be serious (cirrhosis). However, some people with AAT deficiency stay healthy throughout their lives.

WHAT CAUSES AAT DEFICIENCY?

Our bodies are made up of cells. Cells contain genes which are our inherited instructions for health, growth and development. We inherit one copy of each gene from each parent so that we each have two copies of the AAT gene. The AAT gene can come in 3 main forms: M, S and Z. How much AAT we produce is determined by which forms of the gene we have as both AAT genes work together.

M is the commonest form of the AAT gene and people with two M genes have normal levels of AAT. The Z form of the gene is associated with very low protective levels of AAT. A third form is S which is associated with intermediate AAT levels which usually do not affect someone's health.

People with two Z genes only produce about 15 percent of the normal amount of AAT. These levels are not fully protective and this gradually leads to lung damage. Smoking accelerates this progress. Children born with the ZZ combination (or genotype) of the AAT gene forms may have prolonged jaundice. A small proportion of these children may go on to develop liver damage and, in some cases, this can be

severe (cirrhosis). Adults with this combination are also at risk from AAT related liver disease.

CAN AAT DEFICIENCY BE TREATED?

There is no cure for AAT deficiency and it is not possible to repair the Z form of the gene. The best way to prevent symptoms is to avoid smoking. COPD may be treated with medicines similar to those used for asthma. Severe liver disease in childhood and adulthood may need to be treated with liver transplantation.

TESTING FOR AAT

A blood sample can be analysed to measure AAT levels. Blood can also be tested using a laboratory test known as 'immunoelectrophoresis' to work out which combination of the AAT genes (M, S or Z) a person has. This latter test may sometimes be done by looking at the genetic code (DNA) itself.

HOW IS AAT INHERITED?

As we each have two copies of the AAT gene, it follows that there are several combinations of the different AAT gene forms that someone can be found to have on testing. These are MM, MS, MZ, SS, ZS and ZZ.

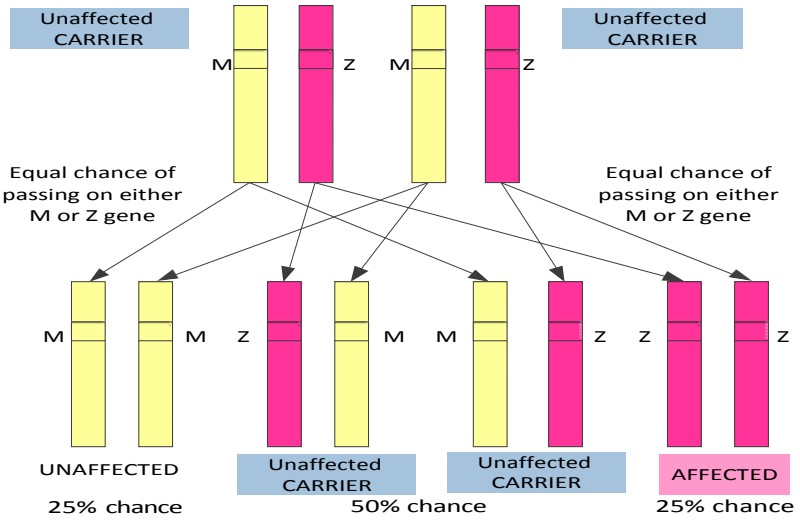
Whether or not we develop symptoms of AAT is largely determined by the forms of the AAT gene we inherit from our parents. We randomly pass on one copy of each pair of our genes to our children. A person with MM genes can therefore only pass on an M gene. A person with MS or MZ gene combination can pass on their M gene or the S or Z gene. A person with two altered genes (ZZ or SS) can only pass on a Z or S gene. A healthy person who carries one copy of the Z gene is said to be a carrier. Approximately 2-5% of people with North Western European ancestry are carriers.

WHAT IF BOTH PARENTS ARE CARRIERS (MZ)?

Parents who are both carriers of AAT deficiency have a risk of having a child with the ZZ gene combination who is at risk of developing symptoms of AAT in childhood or adulthood (Figure 1). For such a couple, each child has a:-

- 25% chance of inheriting the MM combination or genotype (unaffected);
- 50% chance of being a carrier of AAT deficiency (MZ combination);
- 25% chance of being affected with AAT deficiency (ZZ combination

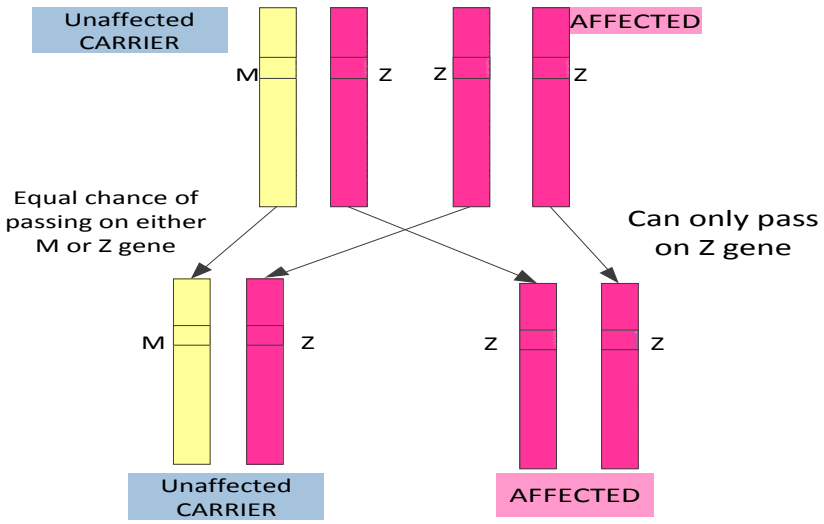
Figure 1



WHAT IF ONE PARENT HAS AAT DEFICIENCY?

In cases where one parent is affected (ZZ), the risk to their children depends on whether their partner is a carrier. If their partner is not a carrier (MM) then all of their children will be carriers (MZ). If their partner is a carrier (MZ) then each child has a 1 in 2 chance of inheriting the MZ or ZZ combination of the forms of the AAT gene. (Figure 2)

Figure 2



THE S FORM OF THE AAT GENE

People who have the SZ combination of the AAT gene forms do not usually experience more lung or liver problems compared to the general population but are at increased risk of COPD if they smoke. MS carriers are usually healthy.

FOR MORE INFORMATION

If you need more information, please contact your local Genetics Department:

South East of Scotland Clinical Genetic Service:	MMC, Western General Hospital Crewe Road South, Edinburgh EH4 2XU Telephone: 0131 537 1116
North of Scotland Genetics Service:	Department of Clinical Genetics Ashgrove House, Foresterhill Aberdeen AB25 2AZ Telephone: 01224 552120
East of Scotland Genetics Service:	Human Genetics Unit Level 6, Ninewells Hospital Dundee DD1 9SY Telephone: 01382 632035
West of Scotland Genetics Service:	Level 2A Laboratory Medicine The Queen Elizabeth University Hospital 1345 Govan Road, Glasgow G51 4TF Telephone: 0141 354 9201

Factual information presented in this communication is based on accurate contemporaneous peer reviewed literature. Evidence of sources can be provided on request.