

Alpha-1 Antitrypsin Deficiency

Alpha-1 antitrypsin (often written as Alpha-1 AT) is one of the many proteins and related substances the body makes from food. It is produced mainly by the liver and circulates around the body in the bloodstream. Although its role is not fully understood, research shows it has a role in preventing tissue damage from the over activity of enzymes called proteases. The body makes proteases in response to infections and irritants entering the body. Without the protective effect of sufficient Alpha-1 AT, proteases may cause tissue damage over a period of many years, particularly in the lungs.

Individuals with Alpha-1 Antitrypsin Deficiency (Alpha-1 ATD) produce a slightly different form of Alpha-1 AT protein in the liver, which becomes trapped there, so that individuals usually, but not always, have low concentrations of Alpha-1 AT in their blood.

The effects of this deficiency vary:

- some people have no ill effects whatsoever
- others remain healthy for years then in their late twenties or more develop emphysema
- some children develop inflammation of the liver which can cause damage. This often becomes apparent when the baby is in the first four months of life with typical signs of jaundice, yellow urine, pale stools, poor weight gain etc.
- in some children the deficiency may not cause significant liver problems until the child is older.

There is no cure for Alpha-1 ATD or specific treatment. Care is centred on dealing with the consequences of liver damage and maintaining a good nutritional status.

What is the future for a child with Alpha-1 ATD?

There is a variable outcome for children with Alpha-1 ATD. A large study in Sweden showed that approximately 15% of Alpha-1 ATD children had problems with liver disease in infancy. Follow up studies in the UK indicate:

- 25% Had no disease symptoms at the age of 10

- 45% Had continuing but variable evidence of liver disease in their blood results
- 5% Needed a liver transplant in the first year of life
- 25% Needed a liver transplant at some point in their childhood

On a worldwide basis there is interest in understanding Alpha-1 ATD and trying to find new therapies for treatment. These include searching for gene therapy and cell transplantation for the condition. At the recent AASLD meeting in Boston there was a symposium on Alpha-1 Antitrypsin Deficiency where leading world experts, including those from the UK, took part in the debate.

Further research is needed

CLDF has awarded grants for two new research projects to be undertaken at a total cost of £173,407.

Project 1

Distribution of haplotypes of alpha-1 antitrypsin in PiZ deficiency - investigating whether a haplotype is associated with liver disease

Applicants: Professor N Kalishchek, Professor R Stockley, Dr K Morgan, Dr N Hadzic

Research Establishment: Institute of Genetics, Queens Medical Centre, Nottingham

Cost: £73,429 over two years

Project 2

RNA inhibitor (RNAi) as an approach for the prevention of liver cirrhosis in patients with the Z mutation of Alpha-1 antitrypsin deficiency

Applicants: Professor John Fagan, Dr Louise Collins, Dr Anil Dhawan

Research Establishment: Department of Clinical Sciences, Guy's, King's and St Thomas' School of Medicine, London

Cost: £99,978 over two years

If anyone would like a copy of the Layman's summary for these projects, please call Catherine on 0121 212 3839.

You can be a Research Champion

To make a real difference CLDF must be in a position to fund at least two projects per year at a cost of £300,000 minimum. This figure equates to a cost of £4.10 for every new child diagnosed with a liver disease.

Many of the children who are being treated effectively today are able to do so as a result of the major advances in knowledge brought about through research, much of which has been funded by CLDF. The average cost of a three year research project is £100,000. To fund a project CLDF needs to have all the money available before making an award.

Individual Cost:

£4.10 Research Champion package

Total Cost:

£300,000 per annum to fund two new projects per year

Contact Catherine Anley on
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Emma Gorman, who was born with Alpha-1 antitrypsin deficiency, pictured with her father, has won the London Marathon to raise funds for CLDF. The 2003 marathon was held on the same day as Emma's birthday in 1997. Photo courtesy of the Nottingham Evening Post.